SPATIO-TEMPORAL ANALYSES OF LEPTOSPIROSIS AT REGIONAL AND PROVINCIAL SCALES IN THAILAND

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การวิเคราะห์เชิงพื้นที่-เวลาของโรคเลปโตสไปโรซิสระดับภาคและระดับจังหวัด ในประเทศไทย

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วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญาวิทยาศาสตรดุษฎีบัณฑิต
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SPATIO-TEMPORAL ANALYSES OF LEPTOSPIROSIS AT REGIONAL AND PROVINCIAL SCALES IN THAILAND

Suranaree University of Technology has approved this thesis submitted in partial fulfillment of the requirements for the Degree of Doctor of Philosophy.

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เลปโตสไปโรซิสเป็นโรคประจำถิ่นของหลายจังหวัดในประเทศไทย โดยเฉพาะอย่างยิ่งจังหวัดในภาคตะวันออกเฉียงเหนือ ในปัจจุบันนี้การศึกษาวิจัยเกี่ยวกับรูปแบบการกระจายเชิงพื้นที่และเชิงเวลารวมทั้งปัจจัยที่สัมพันธ์กับโรคนี้ในประเทศไทยยังมีน้อยอยู่ การวิจัยนี้มุ่งที่จะศึกษาให้เข้าใจในประเด็นเหล่านี้โดยการประยุกต์เทคโนโลยีภูมิสารสนเทศและสถิติเชิงพื้นที่มาใช้ในการวิเคราะห์ข้อมูลอุบัติการณ์ของโรคเลปโตสไปโรซิสในระหว่างปีพ.ศ. 2546 ถึง 2552 การวิเคราะห์สำรวจข้อมูลเชิงพื้นที่ถูกนำมาใช้ในการแสดงรูปแบบการกระจายของโรค สถิติสแกนของคุลดอร์ฟถูกใช้ในการวิเคราะห์หากลุ่มเชิงพื้นที่ เชิงเวลา และเชิงพื้นที่-เวลาของโรคเลปโตสไปโรซิสที่มีนัยสำคัญในประเทศไทย และใช้การวิเคราะห์การถดถอยแบบปัวซองถ่วงน้ำหนักทางภูมิศาสตร์ในการหาการแปรผันของความสัมพันธ์เชิงพื้นที่ระหว่างปัจจัยสิ่งแวดล้อมและโรคเลปโตสไปโรซิสที่อุบัติขึ้นในภาคตะวันออกเฉียงเหนือ ผลการวิจัยพบว่าอุบัติการณ์ของโรคเลปโตสไปโรซิสในภาคตะวันออกเฉียงเหนือสูงกว่าภาคอื่น ทั่วทั้งประเทศไทยนั้นสามารถจัดกลุ่มของอุบัติการณ์โรคเชิงพื้นที่ได้ 7 กลุ่ม และกลุ่มเชิงพื้นที่-เวลาได้เป็น 11 กลุ่ม มีกลุ่มเชิงเวลาเพียง 1 กลุ่มในช่วงที่มีแพร่กระจายสูงของปี 2552 กลุ่มเชิงพื้นที่และกลุ่มเชิงพื้นที่-เวลาที่สำคัญที่สุดอยู่ในพื้นที่ภาคตะวันออกเฉียงเหนือ ส่วนผลวิเคราะห์การถดถอยแบบปัวซองถ่วงน้ำหนักทางภูมิศาสตร์พบว่าปริมาณพื้นที่น้ำท่วมขัง ความหนาแน่นของประชากรเกษตร ปริมาณน้ำฝนรายเดือน และจำนวนวันฝนตกในหนึ่งเดือน มีความสัมพันธ์กับอุบัติการณ์โรคเลปโตสไปโรซิส และความสัมพันธ์นี้แปรผันไปตามพื้นที่อย่างมีนัยสำคัญ การศึกษานี้ให้ข้อเสนอแนะว่าภาคตะวันออกเฉียงเหนือเป็นพื้นที่สำคัญที่มีโรคนี้เป็นโรคประจำถิ่นซึ่งจำเป็นต้องมีการเฝ้าระวังอย่างใกล้ชิด

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LEPTOSPIROSIS/ SPATIAL EPIDEMIOLOGY/ GEOINFORMATICS/ SCAN STATISTICS/ GEOGRAPHICALLY WEIGHTED POISSON REGRESSION/ THAILAND

Human leptospirosis is endemic in many provinces of Thailand, especially in its northeastern region. At present, little is known about spatial and temporal pattern and factors related to the disease in this area. The current research applied geoinformatic technology and spatial statistics to analyze leptospirosis incidence data in Thailand during 2003-2009. Exploratory spatial data analysis was done to demonstrate geographical distribution of the disease. Kulldorff's scan statistic was used to detect significant spatial clusters, temporal clusters and spatiotemporal clusters of leptospirosis in Thailand. Geographically Weighted Poisson regression (GWPR) analysis was used to determine the variations of spatial relationships among a set of environmental variables and leptospirosis incidences in northeast region. The results revealed that leptospirosis was more prevalent in northeast region than the others. Seven significant spatial clusters and 11 spatiotemporal clusters were detected. The most likely spatial cluster and the most likely spatiotemporal cluster were located in the northeast region. There was only one significant temporal cluster identified during the high peak of leptospirosis in 2009. The GWPR analysis showed that amount of actual inundated areas, agricultural population density, amount of monthly rainfalls and numbers of rainy days in a month were related to leptospirosis incidences, and such relationships were significantly varied over space. This study suggests that northeast region of Thailand is an important endemic area of leptospirosis in Thailand which requires a closer surveillance.

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CHAPTER I

INTRODUCTION

1.1 Background and significance of the study

Leptospirosis is a zoonotic disease caused by spirochete bacteria of the genus *Leptospira*. Vertebrate animals including humans are affected by this disease. Leptospirosis infection can occur world-wide, except the areas with enduring snow or ice and desert, but is more common in the tropics than in temperate regions (Levett, 2001), and in either urban or rural environments of both industrialized and developing countries (Bharti et al., 2003). Many kinds of wild, domestic and farm animals can be infected by this organism but the most powerful reservoirs belong to the rodents group (Michel, Branger and Andre-Fontaine, 2002). Infected animals carry the *Leptospira* bacteria in their kidneys and shed the organisms in their urine. Animals infected with the pathogens may or may not have symptoms. Asymptomatic or sub-clinical infection in human is possible and common in endemic area (Tangkanakul et al., 2000). Water, food, or soil contaminated with urine from the infected animals can be the sources of infections to human and other susceptible animals. The most common reservoir hosts are rodents and domestic animals. The human infections may happen by swallowing contaminated foods and water as well as through eyes or nose or broken skin contact with the contaminated environments. It can be an occupational hazard for many people who work with soil, water and animals, e.g., agriculturists (especially paddy rice farmer), aquaculture workers, veterinarians, sewer workers, livestock farmer workers, soldier or patrol policemen. Outbreaks often occur after heavy rainfall during floods (Gubler et al., 2001). Many reported outbreaks of human leptospirosis are usually occurred by exposure to contaminated water.

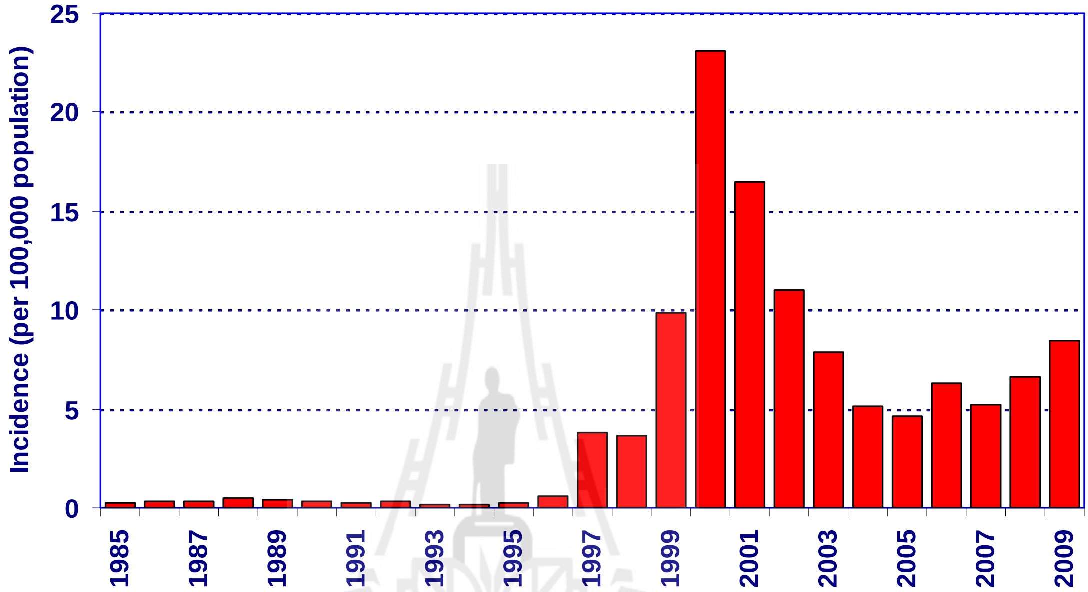


Figure 1.1 Annual Incidence Rates of Leptospirosis in Thailand, 1985-2009.

Source: Bureau of Epidemiology, Department of Disease Control, Ministry of Public Health, Thailand (2010).

Leptospirosis has become apparent as a globally important infectious disease since the past decade. It is considered as an important public health problem and is also a notifiable disease in Thailand (Tangkanakul et al., 2005). It was re-emerging in 1997 (Figure 1.1) with the annual incidence rate of approximately 6 times increased from the baseline (from 0.6 per 100,000 in 1996 to 3.8 per 100,000 in 1997). The incidence continued to be increasing and reached the highest peak in the year 2000 which infected 14,285 Thai people (23.1 per 100,000). After 2000, the incidence rates showed the decreasing trend until 2005, then they were slightly increasing from 2006 to 2009. Nowadays it still remains a public health problem in Thailand, especially in the northeast region. Figure 1.2 showed that the incidence rates of leptospirosis in northeast region were higher than the others every year.

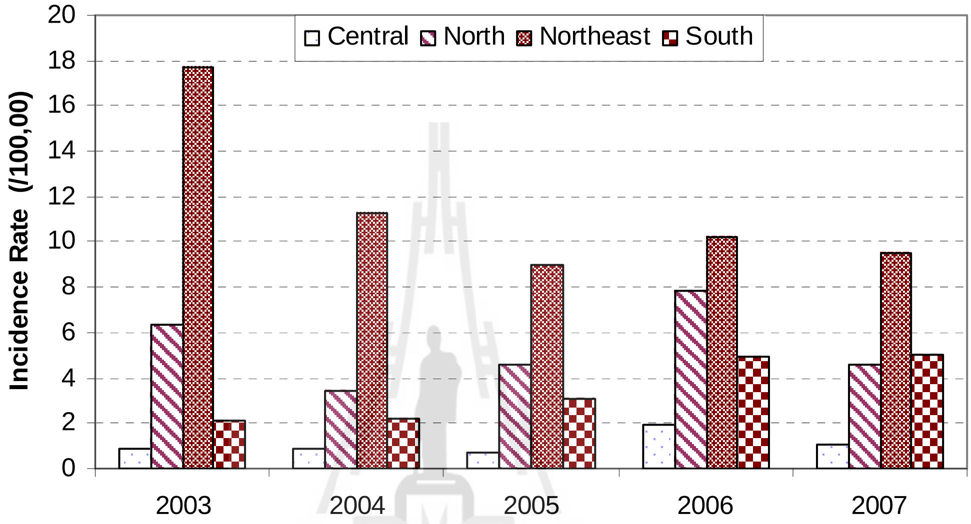


Figure 1.2 Annual Incidence Rates of Leptospirosis in Thailand by region, 2003-2007.

Source: Bureau of Epidemiology, Department of Disease Control, Ministry of Public Health, Thailand (2007).

Epidemiology is the study of distribution and determinants of diseases or health-related events in specified population. Knowledge on epidemiology of the disease plays an important role in public health administration. It provides information on how disease is distributed as well as on the factors that influence such distribution. Applications of geographic information system (GIS), remote sensing (RS) and spatial statistics in epidemiological study can help in better understanding the distribution of a particular disease. Information on locations of disease clusters and the variation of disease frequency over space and time are very important for the formulation of preventive strategies (Nobre and Carvalho, 1996; Ostfeld, Glass and Keesing, 2005). Allocation of the proper prevention and control measures to the right places and time can effectively lessen transmission of the disease as well.

Recently, there are increasing utilization of GIS technology, remote sensing data and spatial statistical methods in epidemiological studies of many infectious diseases (Bailey, 2001; Cline, 1970; Odoi et al., 2004; Rushton, 2003) including malaria, dengue hemorrhagic fever, viral encephalitis, and so on, but there were very few research that focused on leptospirosis. Satellite remote sensing can be a good source of data for the assessment of environmental variations. Environmental conditions are important for pathogens and vectors of many infectious diseases including leptospirosis. The *leptospira* bacteria require moist and warm environmental conditions with the optimum pH of soil, mud, and surface water about 7.0. They can survive for months in muddy water with optimal condition. Vegetation cover and soil moisture are the factors influencing on habitats of rodent reservoirs and the transmission of the infections frequently depend on rodent population density, which, in turn, depend upon environmental conditions and available food (Gubler et al., 2001). Some relevant information can be derived from remotely sensed data and should be used as the factors input in models to test whether they are associated to leptospirosis occurrence.

The motivation behind this research is that incorporation of knowledge from various subjects is an effective way for problem solving. The investigator believes that using geoinformatics together with epidemiologic methods in the study of dieases transmission can discover the knowledge that lead to better understanding of a particular disease.

1.2 Objectives of the study

1.2.1 General Objective

The current research aims to demonstrate the usage of geoinformatic technology (geographical information system and remote sensing) together with spatial statistics for conducting spatial and temporal epidemiological study of human leptospirosis in Thailand with the emphasis on the northeast region.

1.2.2 Specific Objectives

i) To demonstrate and produce maps of spatial and temporal distributions of leptospirosis in Thailand between 2003 and 2009

ii) To ascertain the significant spatial clusters, temporal clusters, and spatiotemporal clusters of leptospirosis incidence in Thailand between 2003 and 2009.

iii) To identify the predictor variables that related to leptospirosis incidence in northeastern Thailand and display the spatial variations of their relationships as well.

1.3 Study hypotheses

The hypotheses of this study were set up as the followings.

i) There were significant spatial, or temporal, or spatiotemporal clusters of leptospirosis at the provincial scale in Thailand.

ii) There were the spatial variations of the relationships among predictor variables and the incidence of leptospirosis in northeast region of Thailand.

1.4 Assumptions

The major assumption underlying this research is that the numbers of population used as the denominators in this study were acquired from Ministry of Interior based on the *de jure* registration which might not be the same as *de facto* population. The actual population in each province seems to be unequal to the registered population due to the migration to other cities for many reasons included job finding. In 2007, the migration rates of Thai people in central region, northeastern region, northern region, and southern region were 4.1, 3.4, 3.1 and 2.8 percent, respectively (The National Statistical Office, 2008). About fifty one percent of migrants have migrated among the provinces in their own region. The calculations of incidence rates using the number of population as the denominators might be a little overestimated, but they seem to be homogenous across the region.

1.5 Scope of the study

The ultimate goal of this study was to find the process that is worth for public health decision makers to use geoinformatics as additional tool for the existing surveillance system. The selected materials and methods used in this study were, therefore, considerably cheap, applicable, and practical for health personnel to carry out.

1.6 Limitation of the study

Leptospirosis cases used for all analyses in this research were based on the notification through the national surveillance system which was possibly under-estimated due to under reporting and sub-clinical infection. The sub-clinical leptospirosis patients with less symptoms might not come to the hospital and were not recorded in the surveillance system. This happening may lead to some information bias.

The remotely sensed data used in the current research were based on the Moderate Resolution Imaging Spectroradiometer (MODIS) sensor on board the TERRA satellite. MODIS data can be downloaded free-of-charge from many websites through the internet. It can be acquired frequently due to its high temporal resolution (1 to 2 days). This is very useful for multi-temporal study concerning the earth surface changes. On the other hand, MODIS produce data at varying spatial and radiometric resolutions (2 bands at 250 m, 5 bands at 500 m and 29 bands at 1 km). This characteristic may result in the limitation of scale of study area to be used with MODIS products.

1.7 Benefit of the study

Analyses of the spatial and temporal components together with the assessment of factors associated to disease incidence are substantially informative. Knowledge or information obtained from spatial epidemiology can increase the potential for public health action. It can help us characterize the spread of the disease in space and time variation. Public health professionals and policy makers at national level or local levels can utilize such knowledge in the formulation and prioritization of prevention and control measures for leptospirosis. These measures can be effectively launched to the specific geographical area (i.e., hotspots), and result in budget saving and appropriate allocation of resources for health system. Moreover, this study can provide initial information for the establishment of leptospirosis early warning system.

1.8 Operational definition

1.8.1 Leptospirosis cases

All leptospirosis cases using in this study were the reported cases through the passive surveillance system of the Ministry of Public Health.

1.8.2 Epidemiological surveillance

Epidemiological surveillance, in general, is the discipline of continuously gathering and analysing data, as well as interpreting information about diseases, and disseminating conclusions of the analyses to relevant organisations.

Surveillance activities can be either “active” or “passive”. Active surveillance is the method that health personnel in the system gathered data by themselves. Passive surveillance is the method that let health care providers report notifiable diseases on a case-by-case basis to the local or central health offices based upon a published list of conditions. This is simple and is minimally burdensome to health care providers.

1.8.3 Exploratory Spatial Data Analysis (ESDA)

Spatial data analysis is an analysis that makes use of geographical component to investigate explicitly spatial aspects of the data. Exploratory Spatial Data Analysis (ESDA) is defined as the collection of techniques to describe and visualize spatial distributions, and determine patterns of spatial association (Anselin, 1999). The results can be displayed in the maps. Thus, using maps to depict geographical distribution of the disease has advantages over the presentation by data tables alone.

1.8.4 Rate smoothing

Rate smoothing is the method for adjusting the raw rate to correct the instability of variances by borrowing strength from other spatial units. The rates calculated from areas with low population usually have higher variance than those calculated from high populate areas. The rates with high variances are likely unreliable. Comparisons of the rates with instability of variances can cause bias results. To solve this problem, one can use the smoothing method of the rates instead of the raw rates. Anselin (2004) suggested the Spatial Empirical Bayes (SEB) method for rate smoothing to be used before the comparison of disease rates.

1.8.5 Disease cluster

Disease cluster is an aggregation of disease cases. Such aggregation can be considered in terms of space, time, or both space and time. Spatial clustering means that a disease has higher incidence rate in some places than in other places. Temporal clustering means that the disease incidence rate is higher at some times than at other times (Rothman, 1990). Clustering in both space and time, which are referred to as space-time clustering or spatiotemporal clustering, means that incidence rates are temporarily higher in some places than the others.

1.8.6 Spatial non-stationarity

Spatial non-stationarity is the condition that occurs when the same stimulus provokes a different response in different parts of the study region. The results of non-stationarity model are appeared to be location dependent. Since one objective of this research was to analyze spatial variations of relationships among predictors and response variable, so spatial non-stationarity was assumed and might be tested. To deal with this circumstance, the local model (instead of global model) was used.

1.8.7 Geographically weighted regression

Geographically Weighted Regression (GWR) is a popular method for detecting and explaining localized deviations from a more general regression fit. GWR has been pioneered by A. Stewart Fotheringham and Martin Charlton (National Center for Geocomputation, National University of Ireland), and Chris Brunsdon (University of Glamorgen, UK). It, as part of local modeling, provides additional analytical tool and a different perspective on spatial analysis. GWR allows the relationship between variables to vary over space by providing separate regression coefficients for every spatial unit in the study area. In conclusion it can be considered that GWR is a localized method of global regression. It disaggregates global statistics by generating a model at each data point.

1.8.8 Poisson regression

Poisson regression applies where the response variable is discrete, e.g., number of cases of a disease, which is not a continuous variable. This model may also be applied to standardized counts or "rates", such as disease incidence per particular number of population. It is assumed that the response variable in this study has a Poisson distribution whose expected value (mean) is dependent on one or more predictor variables. Typically the log of the expected value is assumed to have a linear relationship with the predictor variables.

1.8.9 Geographically weighted Poisson regression

Geographically weighted Poisson regression (GWPR) is the GWR that analyzes the data which the response variable has a Poisson distribution.

1.9 Conceptual framework

The conceptual framework (Figure 1.3) illustrated the steps of data acquisition and data analyses throughout the study. To serve all of the study objectives, the data were analyzed using 3 different computer programs, i.e., 1) Exploratory Spatial Data Analysis (ESDA) using GeoDa Software, 2) detection of disease clusters using SaTScan software, and 3) analysis of spatial relationship using Terraseer STIS software. The output results from these 3 analyses would be the spatial and temporal distributions, spatial clusters, temporal clusters and spatio-temporal clusters of leptospirosis, and the spatial variations of relationships among significant predictor variables and leptospirosis. These outputs can lead to better understanding of spatial epidemiology of leptospirosis which is valuable for health personnel.

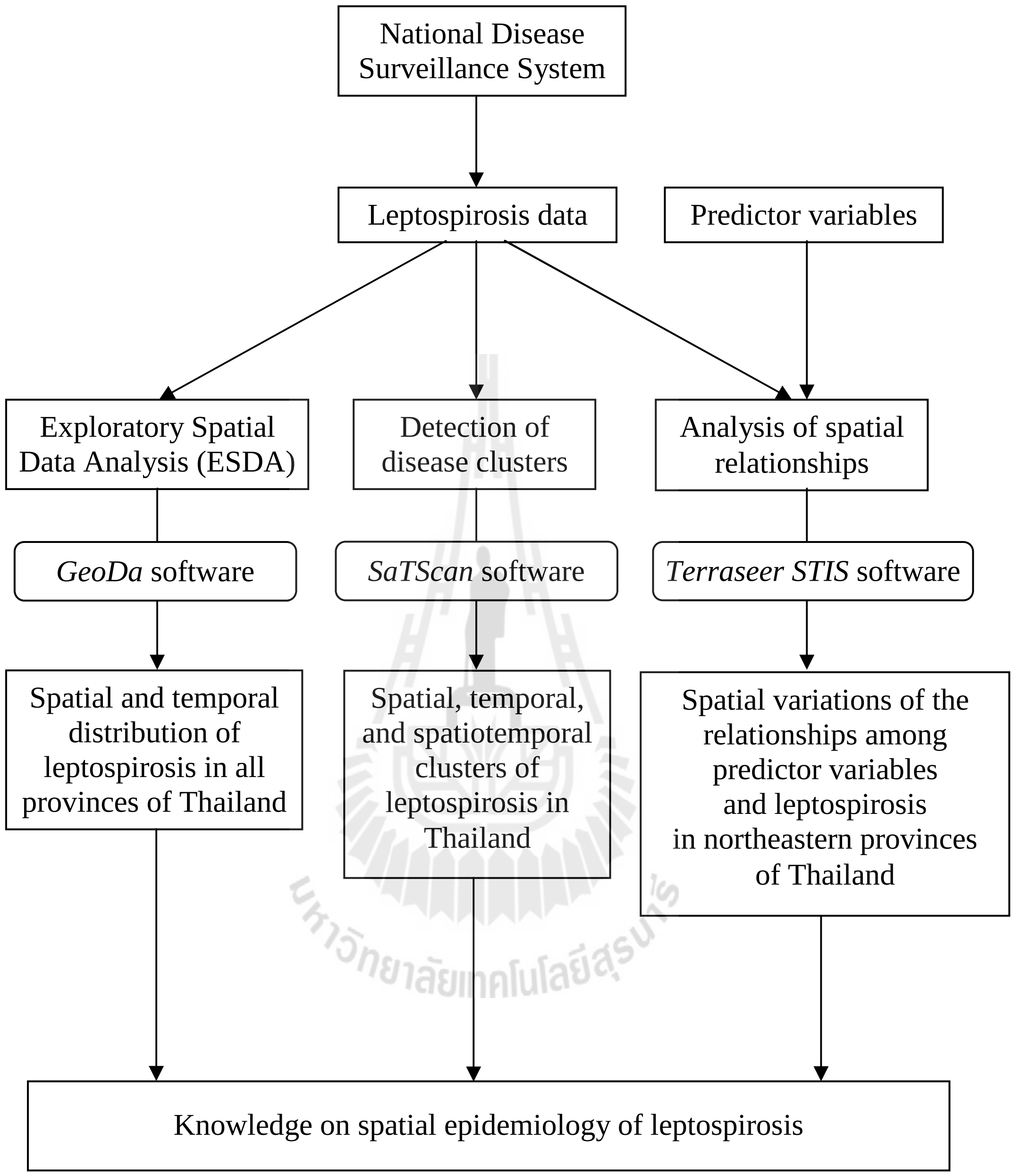


Figure 1.3 Conceptual framework.

CHAPTER II

LITERATURE REVIEW

2.1 History of leptospirosis

The first case of severe icteric illness was reported, and recognized as being new disease, in 1886 by Dr. Adolf Weil of Heidelberg University in Germany. Later, this illness was named as Weil's disease. Many years later, in 1907 the etiologic agent was first examined in kidney tissue of a patient dying during yellow fever outbreak. At that time, a little was known about this agent until 1915, Inada was able to culture the spirochaete bacteria and proved that it associated with Weil's disease (Watt, 1997).

In 1917, the researchers discovered that the rats were the sources of human infection and leptospirosis infection in dogs was recognized at the same time. Leptospirosis in livestock was documented many years later (Levett, 2001). Since then knowledge about reservoir host of leptospirosis was increasingly proposed.

Not only Weil's disease but leptospirosis is also known as Weil's syndrome, canicola fever, canefield fever, nanukayami fever, 7-day fever, Rat Catcher's Yellows, Fort Bragg fever, and Pretibial fever.

2.2 Microbiology

The causal agent of leptospirosis is a spiral-shaped aerobic spirochetes bacteria of the genus *Leptospira* which belongs to the family Leptospiraceae, order

Spirochateales. The size of this organism is 6-20 μm long and 0.1 μm in diameter with 18 or more coils per cell (Figure 2.1). They tend to stain poorly with common laboratory stains and are best visualized by dark field microscopy, silver stain or fluorescent microscopy. Before 1989, the genus *Leptospira* was divided into two species, *Leptospira interrogans* and *Leptospira biflexa* (Levett, 2001). The species *L. interrogans* comprises all pathogenic strains while *L. biflexa* contains the non-pathogenic strains. Recently, the taxonomic studies based on DNA hybridization can divided the genus *Leptospira* into 20 species (Bharti et al., 2003). The species that causes illness to man is *L. interrogans*. More than 200 serovars of *L. interrogans* have been identified. *Leptospira* can survive in mud, moist soil and water for months under the suitable environment. The incubation period of leptospirosis is as short as a few days to as long as 30 days with the average of 15 days (Bureau of Epidemiology, Department of Disease Control, Ministry of Public Health, Thailand, 2009).

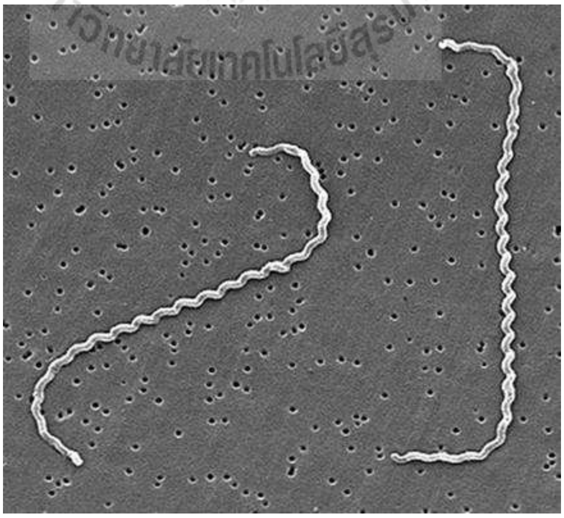


Figure 2.1 Electron micrograph of Leptospiral bacteria.

Source: Levett, 2001.

2.3 Life cycle of pathogenic Leptospires

Leptospires (Leptospiral bacteria) are thought incapable of penetrating normal skin. They enter hosts through damaged skin, mucous membranes, conjunctiva and the lungs by inhalation of aerosol droplets containing the bacteria. They are not spore-forming and die when they are once dehydrated in the dry environment, They migrate to bloodstream and lymphatic system of the host immediately after their entry and, then, spread throughout the host body within short time. Many kinds of animals are reservoir hosts but rats play a major role (The Leptospirosis Information Center, n.d.). The diagram in Figure 2.2 displayed the life cycle of this bacteria.

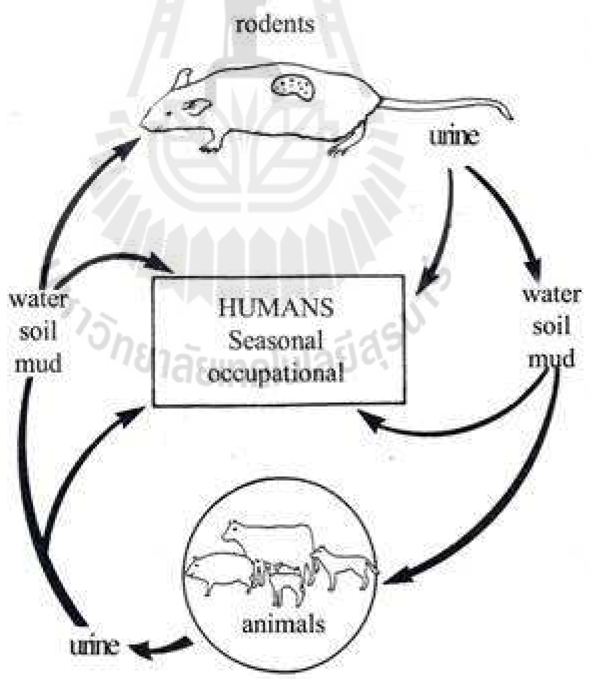


Figure 2.2 Life cycle of pathogenic leptospires.

Source: Faine et al., 1999.

2.4 Clinical manifestation

Leptospirosis infection can occur wherever there is a risk of direct or indirect contact with the urine of infected animals or water and mud contaminated with them. The spectrum of symptoms of leptospirosis is considered broad. The disease in humans is characterized by an acute febrile illness followed by mild self-limiting illness or an even more severe, and often fatal, multi-organ involvement. In the animals, leptospirosis infections are often asymptomatic. In summary, there are two clinical forms of leptospirosis based on severity of the disease, i.e., 'non-icteric' leptospirosis and 'icteric' leptospirosis.

Non-icteric leptospirosis, a self-limiting illness, is a mild form and more common. About 85% to 90% of the cases were non-icteric. The patients with non-icteric form might probably not seek medical attention. Most of them present with a febrile illness of sudden onset (Levett, 2001).

Icteric leptospirosis is a severe form and fatal which occurred less frequently (approximately 10 percent of the cases) and is commonly known as Weil's disease. Icteric leptospirosis may involve internal organs such as kidney, vascular system and liver. The complications of these organs can cause death. Deaths are usually associated with renal failure, hemorrhage and severe jaundice (Douglin et al., 1997).

2.5 Factors contributing to leptospirosis infections

Leptospirosis is closely related to climate, especially rainfall (Kupek, de Sousa Santos Faversani, and de Souza Philippi, 2000; Maciel et al., 2008). Surface water is most important vehicle for transmission of the infection agent, *leptospira* bacteria, to man. Heavy rains produce the expansion of flooded lands. Flooding can amplify the spread of leptospirosis. *Leptospira* can comfortably survive in water and muddy soil environment especially in paddy rice field. A typical feature of paddy fields is that the rice need to grow on flooded soils for a period of time after rice transplanting. This period plays an important role in contamination and transmission of *leptospira* bacteria to farmers or the ones who exposed such contaminated environments. Sasaki et al. (1993) conducted clinic-hospital-based leptospirosis surveillance in the islands of Hawaii. Factors that were associated most strongly with development of leptospirosis were household use of rainwater catchment systems (p-value = 0.003), presence of skin cuts during the incubation period (p-value = 0.008), contact with cattle or the urine of cattle (p-value = 0.05 and 0.03, respectively), and handling of animal tissues (p-value = 0.005). The study of risk factors for leptospirosis during an outbreak in India conducted by Sugunan et al. (2009) revealed that the presence of cattle in the house, drinking stream water, contact with garbage, walking barefoot and standing in water while working were significantly associated with leptospirosis. They found that the stratified analysis showed a dose response relationship between number of cattle in the house and the risk of leptospirosis infection, and also suggested that cattle could be a source of infection.

So far we knew a lot about risk factors of leptospirosis from a vast number of epidemiologic studies. The well-documented risk factors are: age, gender, occupation and some environmental factors (Sasaki et al., 1993; Bunnag et al., 1983; Sundharagiati et al., 1966; Levett, 2001). Prevalence rates of leptospirosis usually increase with age of population. The higher age cause the higher chance of exposure. Susceptibilities to the infections among males and females are not difference. But males have got more infection than female because males seem to experience more risk activities. Agriculturists especially paddy rice farmers are at high risk of indirect contact of animal urines in soil and water. Livestock farmers and abattoir workers are at high risk of direct contact to animal urines. If the animal urines are positive for *Leptospira*, those workers will get infection undoubtedly. Water and mud are the environmental conditions that facilitate the survival of *Leptospira*. Outbreaks of leptospirosis can occur widely after flood (Barcellos and Sabroza, 2001).

Leptospirosis is one of the notifiable diseases by law under the National Communicable Disease Surveillance System in Thailand. The reported cases of leptospirosis are based on both clinical diagnoses made by physicians or and laboratory confirmation followed the guideline of the World Health Organization. Any leptospirosis patients who consulted in-patient or out-patient units will be examined followed the checklist for the likelihood of diagnosis of human leptospirosis (Ministry of Public Health of Thailand, 1999; Kaewpa, 2002). Leptospirosis patients with mild symptoms who did not come to health facilities would not be reported to the system.

Ministry of Public Health of Thailand (1999) reported that most of the cases were rural farmers and age ranged from 15 to 44 years old. The ratio of male to female cases was 2.5. The report from the first Regional Seminar-Workshop in January 2001 in the Philippines revealed that people in Australia, China, Japan, Thailand, Taiwan, India, and Korea are vulnerable to the disease during the harvest and rainy seasons. This occurred when there were increases in rodent population. The farmers in these countries are the most susceptible population.

Globalization could contribute to the dissemination of leptospirosis in the context of international travel, particularly for recreational activities and military expeditions (Pappas et al., 2008). This can make individuals from the developed countries have more chance of exposure to the disease agents.

In summary, the core determinants of leptospirosis transmission are the availability of reservoir hosts or carrier animals, the suitability of environment for survival of infective agent (leptospira) and the interaction between man, animals and environment (Sehgal, 2006). Such interaction was rearranged into a diagram and illustrated in Figure 2.3.

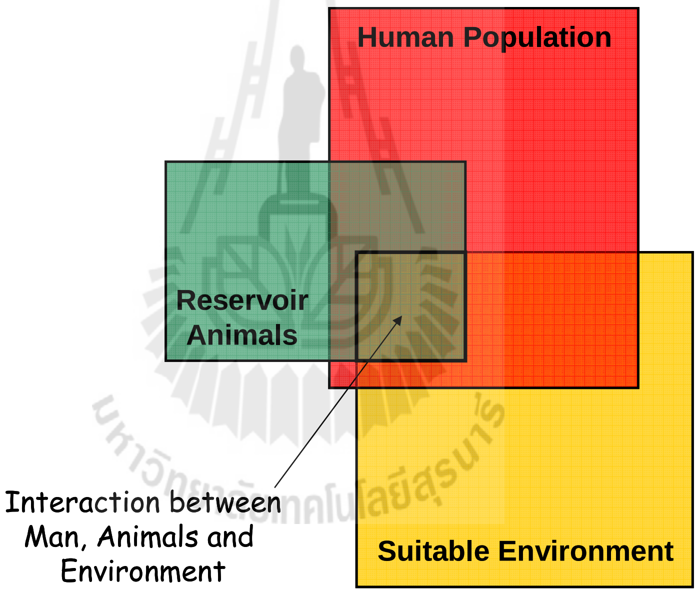


Figure 2.3 The core determinants of leptospirosis transmission.

2.6 Leptospirosis situation

Since leptospirosis is said to be the most wide spread in the world, the clinical cases are regularly reported from almost all continents except Antarctica. Leptospirosis is most common in tropical countries. Even though it is not common in the United State, it has been reported from all regions of the country. In United Kingdom and other European countries, the most common causes of leptospirosis were water-associated and cattle-associated (Arunagiri, 2009).

Southeast Asia is the endemic area of leptospirosis. Human cases of leptospirosis were reported throughout the region (Riccardo and Bayugo, n.d.). All countries in this region have been suffered from leptospirosis. Thailand has been experiencing the highest incidence of leptospirosis in Southeast Asia.

Figure 2.4 Probable occupational exposure to leptospires.

Source: http://www.rd1677.com/branch.php?id=56688

Leptospirosis occurred in every provinces of Thailand but ninety percent of the cases were reported in the northeast region (Tangkanakul et al., 2005). A survey of leptospirosis among rodent reservoirs conducted by Wangroongsarb et al. (2002)

showed that the rodents in northeastern provinces had more positive rate than other regions of Thailand. The temporal variations of leptospirosis in Thailand include a peak incidence in August to September in association with the rainy season. This pattern is often seen in Indian peninsula, southern provinces of China (Sehgal, 2006).

2.7 Spatial pattern of leptospirosis

The successful detection and control of diseases needs to take into account the spatial pattern of disease occurrence and any related risk factors (Pfeiffer et al., 2008). Epidemiologic pattern of leptospirosis has varied from place to place. Many researches have been carried out to gain knowledge about spatial distribution and related factors of many communicable diseases using geoinformatic technology. Among such studies, very few were studied about leptospirosis.

Most recently study by Tassinari et al. (2008) was performed by using scan statistics to detect clusters of urban leptospirosis cases in Rio de Janeiro, Brazil between 1997 and 2002. Six space-time clusters were identified and the cluster cases events were significantly associated with heavy rainfall.

2.8 Spatial statistics in health studies

To date, there are increasing use of spatial statistics to analyze health-related data especially in the study of the relationship of disease and its risk factors. One of those is GWR, a local form of regression used to model spatially varying relationships. GWR is increasingly used instead of the traditional regression technique, such as ordinary least squares (OLS). OLS can be referred to as **global regression** or **aspatial regression**. Global regression models often hide important local variations in model parameters (Tu and Xia, 2008) while GWR models can make more improvement of model performance. Both Global regression and GWR can be applied to various types of models, e.g., linear model, Poisson model and logistic model depending on the types of response variables. In health studies which the outcome variable is discrete number of patients, the Poisson model should be applied.

CHAPTER III

MATERIALS AND METHODS

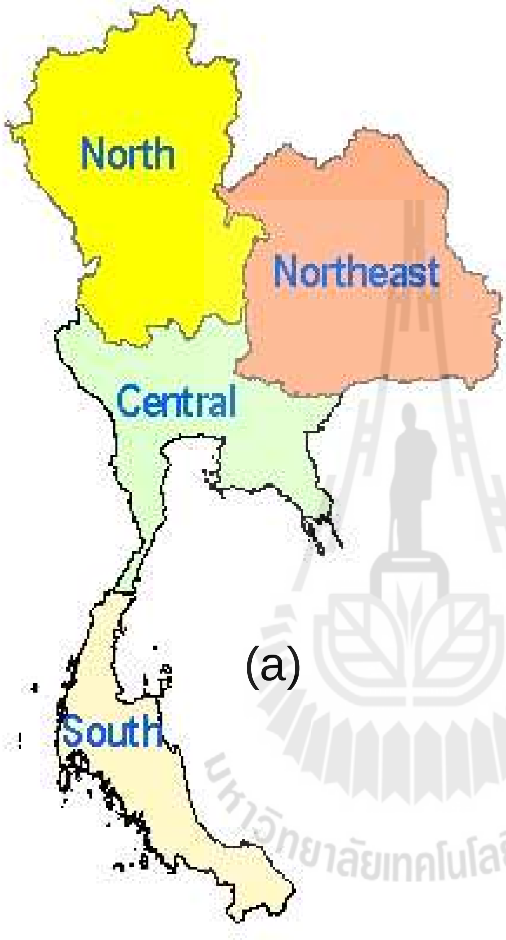
3.1 Study design

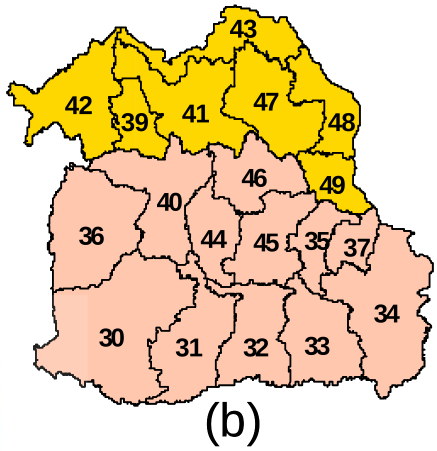
The present research was retrospective epidemiologic study which the outcome of interest, leptospirosis, has already occurred at the time the study was initiated.

3.2 Study area

The study area of this research is a whole Thailand with the emphasis on northeast region. Thailand composes of seventy six provinces with the total area of 513,115 square kilometers. The provinces of Thailand are gathered into 4 regions by location, i.e., central region (26 provinces), north region (17 provinces), northeast region (19 provinces), and south region (14 provinces). Most of the analyses were performed to every provinces in all regions of Thailand but more specific analysis was done with the emphasis on northeast region.

The northeast region comprises 19 provinces with the total area of 168,940 square kilometers. It is separated from Northern and Central Thailand on its west by the Phetchabun mountain range. The northeast region is located on the Korat Plateau, bordered by the Mekong River to the north and east, and by Cambodia to the south. The plateau consists of two main basins, namely, Sakon Nakhon Basin and Korat Basin, which is separated by the Phu Phan mountain range. The population in northeast region as of 2000 was almost 21 millions, one third of total population of Thailand.





Code	Province Name
30	Nakhon Ratchasima
31	Burirum
32	Surin
33	Sisaket
34	Ubon Ratchathani
35	Yasothon
36	Chaiyaphum
37	Amnaj Charoen
39	Nong Bua Lamphu
40	Khon kaen
41	Udon Thani
42	Loei
43	Nong Khai
44	Mahasarakham
45	Roi Et
46	Kalasin
47	Sakon Nakhon
48	Nakhon Phanom
49	Mukdahan

(c)

(a) Thailand map showing 4 regions
(b) Northeast region with the provincial boundaries
(c) Codes and names of provinces in northeast region

Figure 3.1 Maps of the study area.

3.3 Data acquisition and manipulation

3.3.1 Leptospirosis data

Leptospirosis data used in this research were the cases reported to the surveillance system of the Ministry of Public Health. All cases that included in the reports were diagnosed based on specific clinical and laboratory criteria, which then could be classified into 2 types, i.e., *suspected cases* and *confirmed cases*. Suspected case referred to a case that was compatible with the clinical criteria and a screening laboratory diagnosis. The confirmed case referred to a suspected case who had a confirmatory laboratory result.

All records of leptospirosis cases in Thailand from 2003 to 2009 were used in the analyses. The data were aggregated into each province relating to resident locations of the cases. Moreover, leptospirosis data in northeastern provinces in 2007 were selected for the analysis of spatial relationships between a set of geographically referenced environmental factors and leptospirosis incidence.

3.3.2 Spatial data

Topographic maps (series L7018) at the scale of 1:50,000 pertaining to all provinces of Thailand, prepared by Royal Thai Survey Department were used for all spatial analyses. The maps of administrative boundaries were used as the based maps. Centroid maps from Thailand provincial boundary maps were constructed and used in the analysis for disease clustering. Map of water bodies in northeast region was used as the reference in the accuracy assessment of inundated areas extracted from MODIS images.

3.3.3 Remotely sensed data

Multi-temporal cloud-free 10-day composite images were acquired from the Moderate Resolution Imaging Spectroradiometer (MODIS) sensor on board the Terra satellite. These images were obtained through FTP server of Institute of Industrial Science (IIS), University of Tokyo, Japan (Takeuchi et al., 2003; Takeuchi and Yasuoka, 2004). All images were already geometrically corrected and registered to the World Geodetic System (WGS 84). Three bands of MODIS images, i.e., band 1 (620-670 nm, red), Band 2 (841-876 nm, near infrared or NIR) and band 6 (1628-1652 nm, short-wave infrared or SWIR) of each 10-day composite from January to December 2007 were needed. A total of 108 images (3 images × 3 composites × 12 months) were downloaded. Images processing were done to these images in order to extract the monthly inundated areas from each northeastern province for subsequently used as the major predictor variable in regression models.

3.3.4 Environmental data

Environmental data used as the independent (predictor) variables in the analysis for the variations of spatial relationships to leptospirosis. Monthly rainfalls and number of raining days in 2007, summarized for northeast provinces were acquired from Department of Meteorology and Department of Royal Irrigation.

Various types of annual agricultural area in square kilometers of each province in northeast region in 2007-2008 were obtained from the Center for Agricultural Technology Transfer and Services, Ministry of Agriculture and cooperatives through the website: http://agtech.doae.go.th/database2/menu.php. The type of agriculture areas used as the predictor variables in regression models included:– a) paddy rice areas, b) crop area, c) horticulture areas, d) livestock areas, and e) aquaculture areas.

Annual numbers of agricultural population by province of northeast region in 2007 were also obtained from the same source as the agricultural area. Density of agricultural population per square kilometer of total agricultural areas was calculated for each province and used as a predictor variable in regression models.

3.4 Data analysis

3.4.1 Exploratory Spatial Data Analysis (ESDA)

First of all, the **monthly incidence rates** from 2003 to 2009 were calculated for each province of Thailand. The incidence rate is the number of new cases per population in a given time period. It is calculated by the division of number of cases by number of populations in a particular province. This incidence rate can be referred to as **cumulative incidence**. If the denominator is the sum of the person-time of the at risk population, this rate will be known as the **incidence density** or **person-time incidence rate**. This research used only the cumulative incidence in all analyses. These incidence rates were, thereafter, referred to as the 'raw incidence rates' because they were simply calculated by using only numerators and denominators.

To avoid the problem of variance instability, the incidence rates were then smoothed prior to making the maps of geographical distribution of leptospirosis. The Spatial Empirical Bayesian (SEB) method was used to smooth the incidence rates before performing the visualization. This smoothing procedure required a spatial weights file to be specified. This weight file was used to impose a neighborhood structure on the data to assess the extent of similarity between provinces and values. The queen contiguity weighting method was used. Therefore, the provinces that either share border or vertex with a particular province were categorized as neighbors.

GeoDa™ v.0.9.5-i, released on August 3, 2004 (Anselin, 2004), were used to calculate the SEB smoothed incidence rates at the provincial scale. Maps of these smoothed incidence rates were created. ESRI® ArcGIS™ 9.0 were used for making maps that visualized the variations of leptospirosis incidence in space and time. The 5-category choropleth map was used as the mapping method for these **raw** and **smoothed** incidence rates.

Furthermore, the "Excess Risk" was calculated for each province and each year during 2003-2009. The excess risk is the ratio of the observed rate to the overall rate computed for all the data. Overall rate is calculated as the proportion of the total sum of all cases over the total sum of all populations (Anselin, 2005). Excess risk of each province can be calculated using equation below:

$$ER_i = IR_i / IR_t \qquad (3.1)$$

The term ERi denotes the excess risk at province i, IRi refers to incidence rate of province i, and IR_t refers to incidence rate of entire study area (Thailand). Provinces with excess risks greater than 1 are the provinces that have higher risks than the overall average. In contrast, provinces with excess risks less than 1 are the provinces that have lower risks than the overall average.

3.4.2 Analyses for leptospirosis clusters

Analyses for spatial cluster were performed to determine the significant local clusters by using spatial scan statistic. Furthermore, temporal clusters and spatio-temporal clusters were evaluated using temporal scan and space-time scan statistics, respectively. SaTScan™ software was used to carry out these analyses. This software was developed under the joint auspices of (i) Martin Kulldorff, (ii) the National

Cancer Institute and (iii) Farzad Mostashari at the New York City Department of Health and Mental Hygiene. In this study, the version 7.0 released on August 14, 2006 (Kulldorff and Information Management Services Inc., 2006) was used. This software can be freely downloaded at http://www.satscan.org/. This method imposes a circular scanning window on the map and lets the center of the circle move over the study area so that at each position the window includes different sets of neighboring administrative areas (Kulldorf, 1997; Kulldorf et al., 1998). For each circle centroid, the radius varies continuously from zero to a user-defined maximum. The test statistic adopted is the likelihood ratio, which is maximized over all the windows to identify the most likely disease clusters.

The number of leptospirosis cases in each province is Poisson-distributed according to a known underlying population at risk. The spatial scan statistic, temporal scan statistic, and space-time scan statistic with Poisson-based model were used to locate the significant spatial cluster, temporal cluster, and spatio-temporal cluster of leptospirosis, respectively. Outputs of these analyses were transferred to ArcGIS software for making the maps.

3.4.3 MODIS image processing

Computer software ERDAS Imagine 9.0 was used to manage the data. Subsets of images that cover the area of northeastern Thailand were prepared for the analyses. Normalized Difference Vegetation Index (NDVI) and Land Surface Water Index (LSWI) images were created using surface reflectance value from each band and calculating according to Equation (3.2) and (3.3), respectively (Xiao et al., 2005; Xiao et al., 2006).

$$NDVI = \frac{\rho_{nir} - \rho_{red}}{\rho_{nir} + \rho_{red}} \tag{3.2}$$

$$LSWI = \frac{\rho_{nir} - \rho_{swir}}{\rho_{nir} + \rho_{swir}} \tag{3.3}$$

An algorithm to identify flooded areas and rice field which developed by Xiao et al. (2005) were applied and mainly used to identify water bodies and other inundated areas through the images of NDVI and LSWI under hypothesis that – a temporary inversion of the vegetation indices, where LSWI either approach to or is higher than NDVI values, may signals flooding in paddy rice field. This algorithm is pixel-oriented which focuses on the period of flooding. According to this algorithm a pixel was classified as water if $NDVI<0.10$ and $NDVI<LSWI$. A procedure for implementation of the algorithm was shown in Figure 3.2.

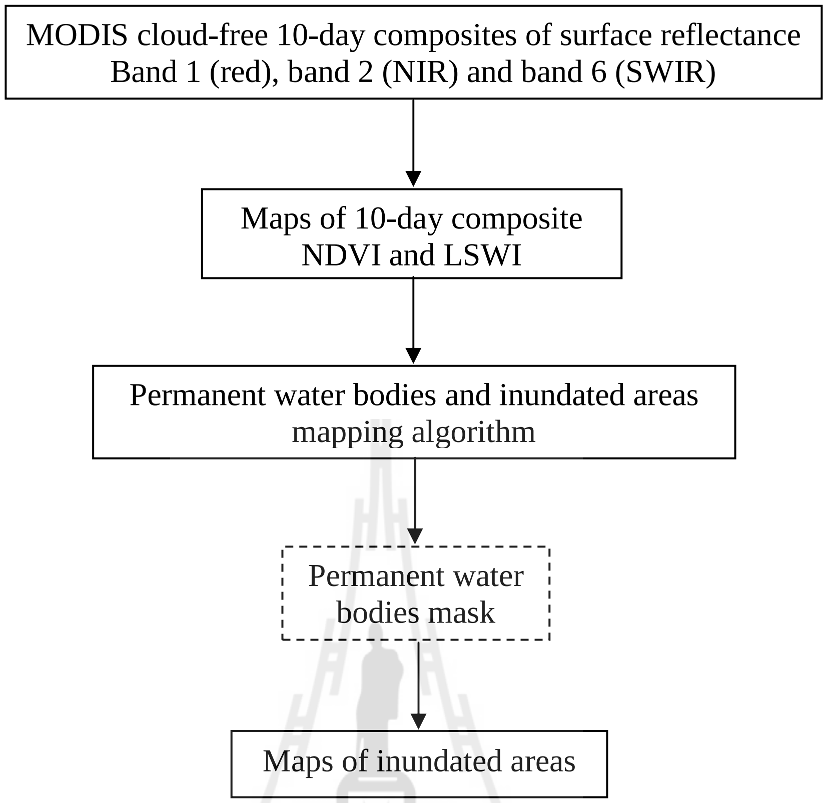


Figure 3.2 Diagram of algorithm for mapping of inundated areas.

The schematic diagram shown in Figure 3.3 illustrates the spatial modeler of ERDAS Imagine 9.0 software for processing the images of NDVI, LSWI, and the water body and other inundated areas. These models facilitated the processing of series of images.

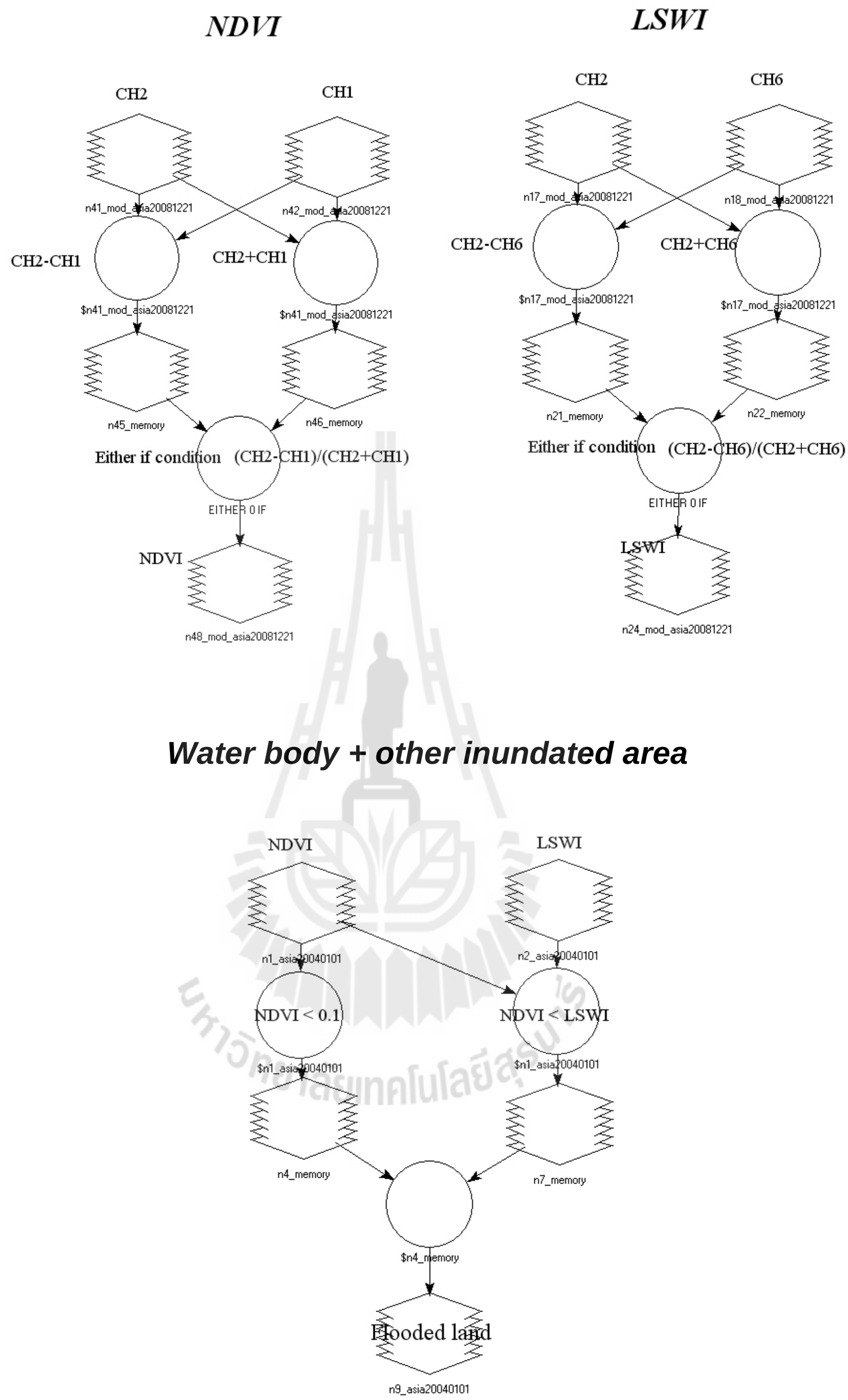


Figure 3.3 Spatial model for processing the images of NDVI, LSWI, and water body plus other inundated areas.

The product images from this algorithm were any kind of water areas included permanent water bodies and other types of inundated areas. Permanent water bodies, in fact, were typically constant over time while other inundated areas were often varied from time to time.

The purpose of this section was to detect the monthly variations or changes of inundated areas which might be one of the important predictors of leptospirosis transmission. The areas of permanent water bodies, therefore, should be removed from the product images. The remaining areas would be inundated areas other than permanent water bodies. For this reason, one mask of permanent water bodies was generated and overlaid to each product image. The final images were obtained after subtracting the permanent water bodies from those images and would be used in further analyses. Therefore the term 'inundated areas' mentioned thereafter was referred to the inundated areas which was already exclusive of permanent water bodies.

A total of 36 maps (3 maps a month) of inundated areas in 2007 were created. Subsequently, provincial boundary map of the study area was overlaid to each image to generate summaries of inundated areas (in sq km) in each month. The average values of those areas from the three maps of each month were calculated for each province. These variables were used as the predictors in regression analysis to test for their spatial relationships to leptospirosis incidence.

3.4.4 Accuracy assessment of image classifications

The accuracy assessment of MODIS flood land products was carried out using a raster map of water body as the reference. This raster map was created by converting from the vector layer of water body from L7018 maps over the same area as the classified image. The cell size of such raster map was set up as 458 meters which was the same as the pixel size of MODIS classified images. The accuracy assessment obtained by using the test function from ERDAS Imagine 9.0 software.

3.4.5 Analysis for spatial relationship between leptospirosis and predictor variables

Geographically Weighted Regression (GWR) was used to test whether the spatial variability of independent variables (i.e., environmental and some other factors) exhibits significant relationship with leptospirosis. GWR is the extension of classical OLS regression. GWR is a kind of local statistics which allows local parameters to be estimated, while OLS is a **global** or **aspatial** regression which assumes the relationship under study is constant over space and the regression coefficient is estimated to be the same for all the study area.

Global regression model can be written as:

$$\log(E(\lambda_i)) = \beta_0 + \beta_1 x_1 + \beta x_2 + \ldots \beta_n x_n + \varepsilon \qquad (3.4)$$

where $\log(E(\lambda_i))$ denotes the logarithm of expected rate of outcome of the i^{th} observation, $x_1 \ldots x_n$ denote the set of independent variables, β_0 denotes the intercept of the model, $\beta_1 \ldots \beta_n$ denote the regression coefficients of independent variable $x_1 \ldots x_n$, and ε denotes the regression residual.

The basic GWR model can be written as:

$$\log(E(\lambda_i)) = \beta 0(u_i,v_i) + \beta_1(u_i,v_i)x_1 + \beta_2(u_i,v_i)x_2 + \ldots \beta_n(u_i,v_i)\, x_n + \varepsilon_I \qquad (3.5)$$

where (u_i,v_i) denotes the coordinate of the i^{th} point in space, $\beta_n(u_i,v_i)$ denotes the regression coefficient of independent variable x_n at point i.

The computer program TerraSeer® Space-Time Intelligence System™ (Terraseer STIS) was used for this analysis. Poisson-based models for global regression and GWR were selected for the reason that the dependent variable in this study (leptospirosis cases) was Poisson-distributed by its nature. Thus, GWR analysis in this study was then referred to as Geographically Weighted Poisson Regression – GWPR (Nakaya, Fotheringham, Brunsdon and Charlton, 2005).

The dependent or response variable used in the GWPR analyses was the number of leptospirosis cases in each province, while the numbers of populations (denominators) were put as the weight dataset in Poisson model type. The independent variables were: - water and flood land area extracted from MODIS (km^2), population density (per km^2), agricultural area (km^2), monthly rainfall (mm), number of raining days in a month, monthly average of minimum temperature, and monthly average of maximum temperature.

The incubation period of leptospirosis varies from a week to a month. The man exposed to risk factors at a time might have got the symptom a week to a month later. The data of some independent variables of a particular month must be, therefore, associated to the data of dependent variable in a month later. So, in this study, independent variables during January 2007 to December 2007 were used to analyze with corresponding to the leptospirosis cases occurred in February 2007 to January 2008, respectively.

Both global Poisson regression and GWPR were performed using leptospirosis case counts as dependent variable and the environmental factors described above as independent variables (Jacquez, n.d.). Firstly, global Poisson models were applied to measure global relationships between dependent and independent variables. All independent variables were put to the model and let the program selected the best subset of variables to be in the final model by using the log likelihood as the model selection criteria. Parameter estimates from the final model were used for the interpretation. Regression residuals of the final model were test for global autocorrelation. Global Moran's I was calculated from TerraSeer STIS software. If there was no autocorrelation of the residuals, the relationships were considered constant over study area. In contrast, if the autocorrelation significantly existed, those relationships were varied spatially and only the local type of regression must be used for the explanation of the variation. GWPR models were applied to the same dataset to determine the local relationships. The independent variables for this GWPR were the same as final model in global Poisson regression. The geographic weighting selected for using in GPWR analysis was a set of 20 nearest neighbors. The regression weight method was set as "equal weight". The centroids of districts of all provinces in northeast region were used as the regression points. Therefore, the regression coefficients of each variable at every district controids were obtained and mapped to show there variations over study area.

CHAPTER IV

RESULTS AND DISCUSSION

4.1 Results

The results were divided into three main parts, namely, i) spatial and temporal distribution of leptospirosis by province in whole Thailand during 2003-2009, ii) spatial clusters, temporal clusters and spatio-temporal clusters of leptospirosis, and iii) spatial variations in the relationship among predictor variables and spatio-temporal dynamics of leptospirosis infection in northeastern Thailand.

4.1.1 Spatial and temporal distribution of leptospirosis

During 2003-2009, a total number of 27,860 cases of leptospirosis were reported to the surveillance system. Sixty eight percent (19,063 cases) were in northeast region, whereas the rest 15%, 11% and 6% were from the North, South and Central regions, respectively. The incidence of leptospirosis in whole Thailand ranged from 4.6 to 8.5 per 100,000 populations (Table 4.1).

Figure 4.1 shows the annual incidence rates of leptospirosis in each region. It reveals that the incidence rates in central and north region appeared to be less varied throughout the study period whilst incidence rates in the south region were gradually increasing year by year from 2003 to 2009. The fluctuation pattern of incidences in northeast region was quite different from the others. The line graph of incidences of northeast region was U-shaped distributed. The high incidence rates were observed at the beginning (2003) and at the end (2009) of study period with the rates of 17.7 and

17.5 per 100,000 population, respectively. The map in Figure 4.2 shows the comparison of leptospirosis incidence rate distribution by region from 2003 to 2009.

Table 4.1 Annual cases and annual incidence rates (/100,000) of Leptospirosis by regions, 2003-2009.

Year	Central		North		Northeast		South		Total	
	Cases	Rate	Cases	Rate	Cases	Rate	Cases	Rate	Cases	Rate
2003	180	0.87	773	6.38	3,829	17.70	180	2.13	4,962	7.88
2004	175	0.85	416	3.48	2,421	11.28	187	2.21	3,199	5.12
2005	145	0.71	540	4.55	1,920	9.02	263	3.10	2,868	4.61
2006	406	1.95	936	7.87	2,177	10.20	422	4.93	3,941	6.29
2007	222	1.06	546	4.59	2,038	9.53	435	5.06	3,241	5.16
2008	213	1.00	491	4.13	2,926	13.66	580	6.67	4,210	6.66
2009	219	0.88	522	4.40	3,774	17.50	924	10.35	5,439	8.47
Overall	1,560		4,224		19,085		2,991		27,860	

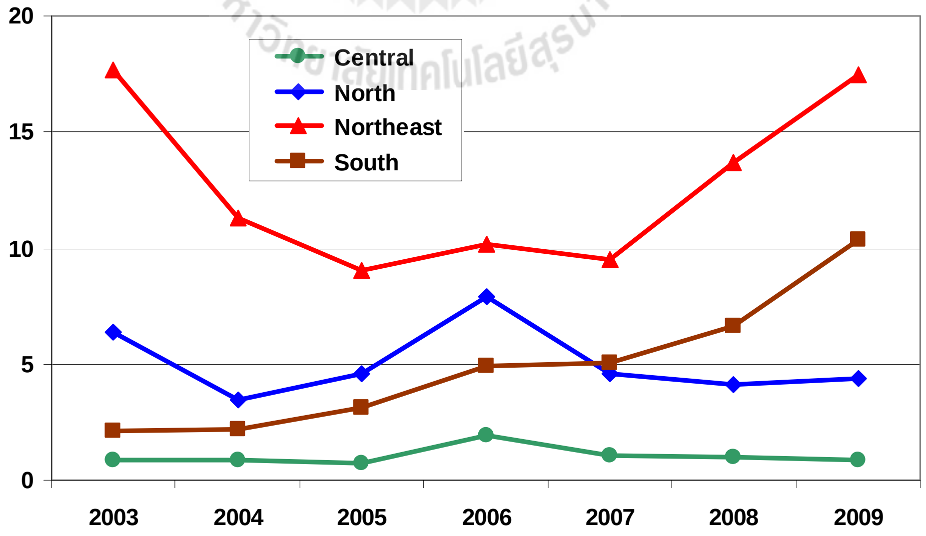


Figure 4.1 Annual incidence rates of leptospirosis by region, 2003-2009.

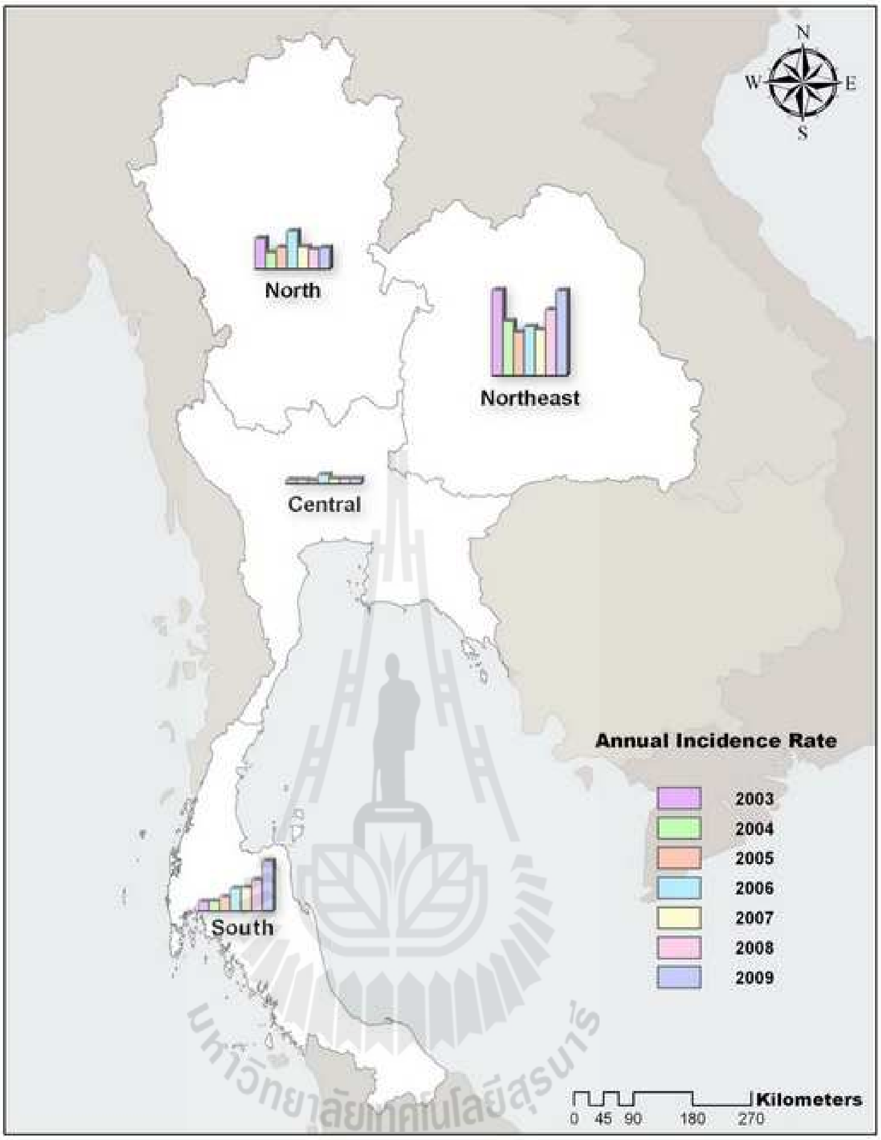


Figure 4.2 Distribution of leptospirosis incidence rates by region, 2003-2009.

The annual incidence rate of leptospirosis of each province of Thailand from 2003 to 2009 was shown in Table 4.2. The province with highest incidence rate in each year was highlighted. The highest incidence rates from 2003 to 2009 were observed in Sisaket, Kalasin, Phayao, Nan, Kalasin, Burirum and Ranong, respectively.

Table 4.2 Annual incidence rates of leptospirosis by province.

Region	Province	Annual Incidence Rate (per 100,000)						
		2003	2004	2005	2006	2007	2008	2009
CENTRAL	Bangkok	0.02	0.09	0.05	0.14	0.04	0.26	0.16
	Samut Prakarn	0.00	0.00	0.09	0.55	0.54	0.00	0.52
	Nonthaburi	0.00	0.32	0.63	0.41	0.10	0.10	0.00
	Pathum Thani	0.55	0.40	0.13	0.12	0.23	0.33	0.00
	Phra Nakhon Sri Ayuthay	1.20	0.40	0.67	3.06	2.39	3.01	3.12
	Ang Thong	2.41	1.74	1.06	1.76	1.06	0.70	1.05
	Lop Buri	0.65	0.79	1.47	2.13	1.20	1.06	0.27
	Sing Buri	0.90	0.90	1.37	7.82	0.46	1.39	0.00
	Chai Nat	8.00	5.21	3.52	9.13	7.96	8.32	7.74
	Saraburi	4.17	2.95	3.17	8.09	1.15	2.91	0.80
	Chon Buri	0.09	0.17	0.26	0.59	0.25	0.56	0.47
	Rayong	4.17	2.36	1.27	6.53	2.44	1.02	0.67
	Chanthaburi	2.36	6.76	3.83	23.39	9.95	11.07	9.65
	Trat	0.00	0.00	0.00	1.37	0.91	1.81	1.80
	Chachoengsao	0.46	0.46	0.46	0.77	0.31	0.30	0.00
	Prachin Buri	0.88	1.56	0.67	0.66	0.44	1.09	0.00
	Nakhom Nayok	1.99	2.40	2.00	0.80	2.00	1.20	0.80
	Sa Kaeo	3.33	3.71	3.91	8.00	7.06	1.48	2.96
	Ratchaburi	0.12	0.85	0.37	0.36	1.33	0.12	0.12
	Kanchanaburi	0.75	1.00	0.37	0.24	0.72	1.79	2.62
	Suphanburi	1.73	1.17	0.95	1.54	1.07	0.36	0.36
	Nakhon Pathom	0.25	0.00	0.25	0.00	0.12	0.00	0.00
	Samut Sakhon	0.00	0.00	0.00	0.22	0.00	0.00	0.21
	Samut Songkhram	0.49	0.00	0.00	1.54	0.00	0.00	1.03
	Phetchaburi	0.65	0.00	0.00	0.44	0.00	0.22	0.00
	Prachuap Khiri Khan	0.82	0.41	0.83	1.02	0.61	0.20	0.60
NORTH	Chiang Mai	1.63	2.10	3.23	4.53	2.41	1.56	3.11
	Lamphun	0.25	0.74	0.99	0.99	1.23	0.00	0.00
	Lamphang	20.53	6.47	7.97	10.96	5.04	5.20	3.26
	Uttaradit	4.14	5.67	4.68	4.06	3.64	4.52	3.66
	Phrae	20.26	10.26	7.62	12.98	5.55	2.80	3.88
	Nan	16.29	10.21	17.79	67.17	16.96	16.57	18.49
	Phayao	19.40	11.72	25.84	21.17	17.48	16.63	14.98
	Chiang Rai	11.01	4.12	3.36	7.43	11.01	7.75	5.30
	Mae Hong Son	2.51	4.56	13.67	10.22	3.92	2.76	4.75
	Nakhon Sawan	1.06	0.64	0.84	1.95	1.77	1.58	2.70
	Uthai Thani	3.55	1.80	5.21	4.90	1.53	5.81	3.05
	Kamphaeng Phet	1.43	0.00	0.00	0.00	0.55	0.69	2.07
	Tak	0.00	0.39	1.35	6.29	1.71	2.06	0.74
	Sukhothai	0.32	0.49	0.49	0.33	0.99	1.32	1.82
	Phitsanulok	4.61	3.39	1.43	2.73	2.25	2.61	4.98
	Phichit	1.01	0.00	0.18	0.90	1.43	1.80	3.79
	Phetchabun	5.83	3.60	2.79	5.09	3.79	3.71	4.12

Table 4.2 (Continued).

Region	Province	Annual Incidence Rate (per 100,000)						
		2003	2004	2005	2006	2007	2008	2009
NORTHEAST	Nakhom Ratchasima	8.12	6.24	4.36	4.15	2.50	3.60	5.22
	Burirum	23.55	13.90	5.43	7.82	12.62	46.98	41.64
	Surin	24.73	26.93	9.54	12.07	11.20	17.25	44.85
	Sisaket	40.42	10.19	16.64	22.70	33.11	22.47	42.67
	Ubon Ratchathani	14.23	6.50	4.81	6.97	5.10	7.20	12.03
	Yasothon	5.42	14.44	11.82	10.90	3.88	3.15	2.60
	Chaiyaphum	10.99	4.70	6.62	6.17	2.06	4.10	5.17
	Amnat Charoen	7.56	7.32	3.80	5.42	4.34	4.88	8.39
	Nong Bua Lam Phu	13.42	11.26	5.65	1.41	2.01	0.60	3.60
	Khon Kaen	31.09	11.96	13.87	19.90	13.48	19.50	19.36
	Udon Thani	6.63	5.16	8.87	5.51	6.61	10.96	13.28
	Loei	22.39	28.67	19.46	18.44	9.78	27.55	33.80
	Nong Khai	11.85	8.84	20.09	20.27	8.45	9.51	7.39
	Maha Sarakhom	14.62	6.07	3.85	4.48	4.69	6.30	9.82
	Roi Et	32.28	10.48	10.30	6.03	4.73	6.27	10.63
	Kalasin	25.90	38.25	15.53	24.01	34.03	38.96	24.32
	Sakon Nakhon	6.93	3.61	6.53	7.95	2.25	2.87	6.63
	Nakhon Phanom	0.28	0.71	0.72	0.14	4.03	1.43	1.14
	Mukdahan	2.36	9.53	4.50	2.09	6.56	2.08	10.67
SOUTH	Nakhon Sri Thammarat	2.87	2.11	2.00	3.12	5.56	15.76	8.33
	Krabi	2.36	0.26	0.51	2.25	1.49	1.45	1.91
	Phangnga	11.25	6.25	11.65	15.61	15.08	24.96	36.81
	Phuket	1.46	1.77	4.15	5.06	6.65	4.98	7.95
	Surat Thani	2.59	1.17	0.85	0.84	1.67	2.56	4.07
	Ranong	7.35	5.30	4.51	29.05	3.34	15.41	123.68
	Chumphon	2.31	4.00	4.43	5.45	1.46	4.97	1.65
	Songkhla	0.86	1.09	4.26	5.50	4.40	4.36	6.51
	Satun	1.10	0.00	0.00	0.36	4.62	2.79	9.71
	Trang	0.99	7.64	5.51	11.08	8.40	4.08	7.64
	Phatthalung	1.59	1.79	1.40	1.79	4.77	4.96	22.77
	Pattani	0.16	0.00	0.16	2.36	6.29	2.81	3.11
	Yala	1.95	2.16	2.60	3.43	2.56	3.17	4.42
	Narathiwat	1.56	2.28	6.60	6.68	8.63	4.47	8.47

Note: The highlighted cells indicate the highest incidence rates.

Monthly fluctuation of leptospirosis incidence rates in Thailand during 2003 and 2009 was showed in Figure 4.3. It illustrates that the highest leptospirosis incidences were occurred during the late rainy season of each year varying around August to October.

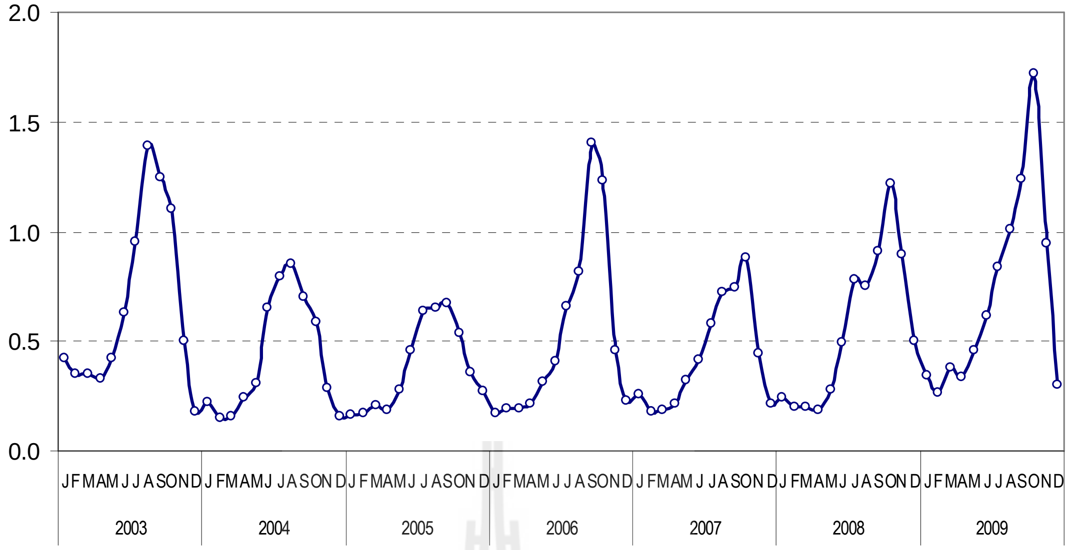


Figure 4.3 Monthly incidence rates of leptospirosis in Thailand, 2003-2009.

Raw annual incidence rate and SEB smoothed incidence rate by province were calculated and mapped in Figure 4.4 and 4.5, respectively. Those maps illustrate few different between raw rates and SEB smoothed rates due to the instability of variances. The interpretation and comparison of leptospirosis incidence between provinces by using raw rates might be done with bias. Using the smoothed rates instead of raw rates is more efficient and less biased. However, both kinds of rates showed similar patterns that leptospirosis incidence rates in northeast provinces were higher than other regions every year. Incidence rates of many provinces of northeast region and some provinces in north region were higher than in the central region and the upper part of south region. Similar patterns were observed in every year throughout the study period. The comparisons between raw and smoothed incidence rates in each province by each year were shown in Figure 4.6 as the maps and in Appendix A as the tables with the values of incidence rates.

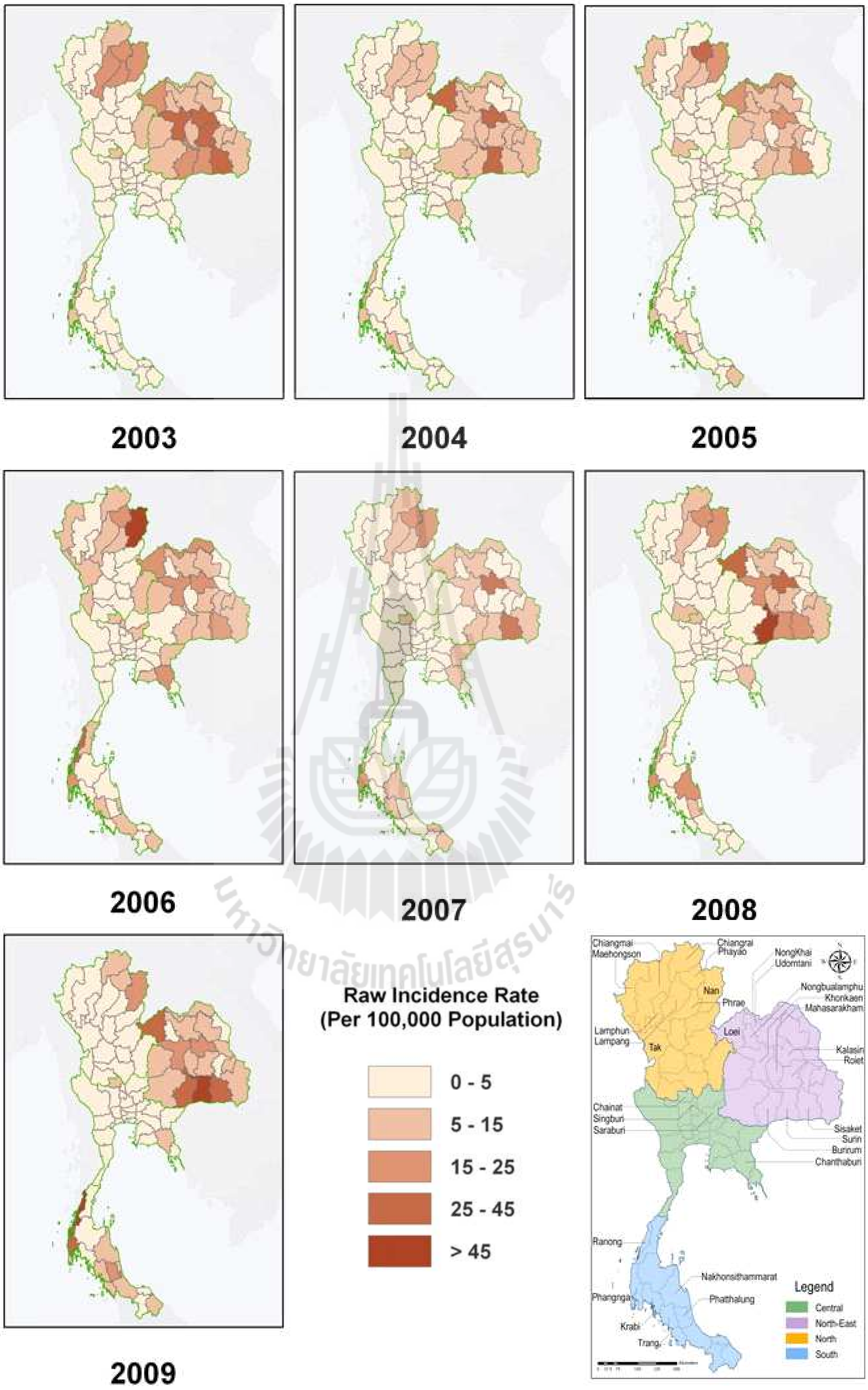


Figure 4.4 Raw incidence rates of leptospirosis by province, 2003-2009.

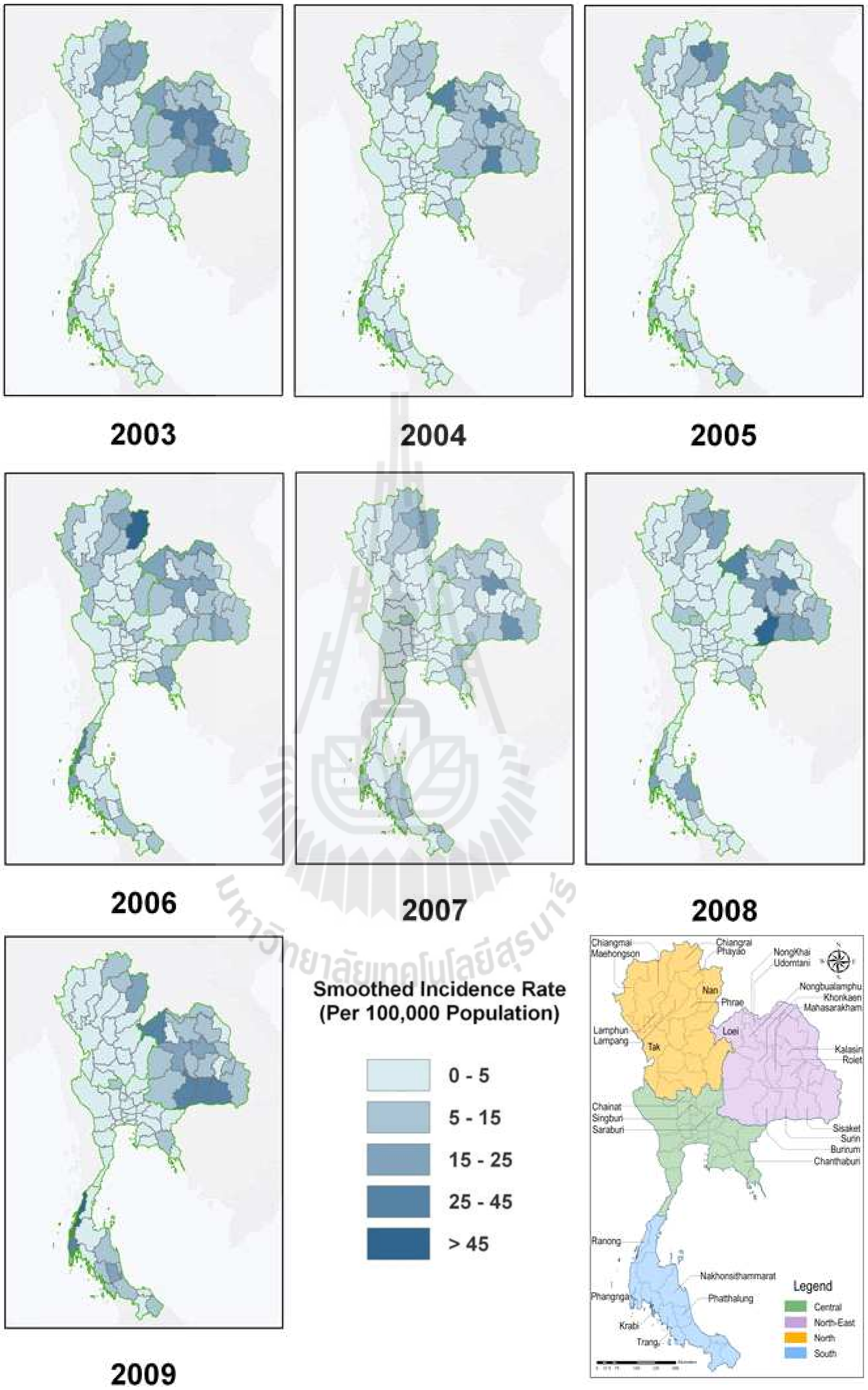


Figure 4.5 Smoothed incidence rates of leptospirosis by province, 2003-2009.

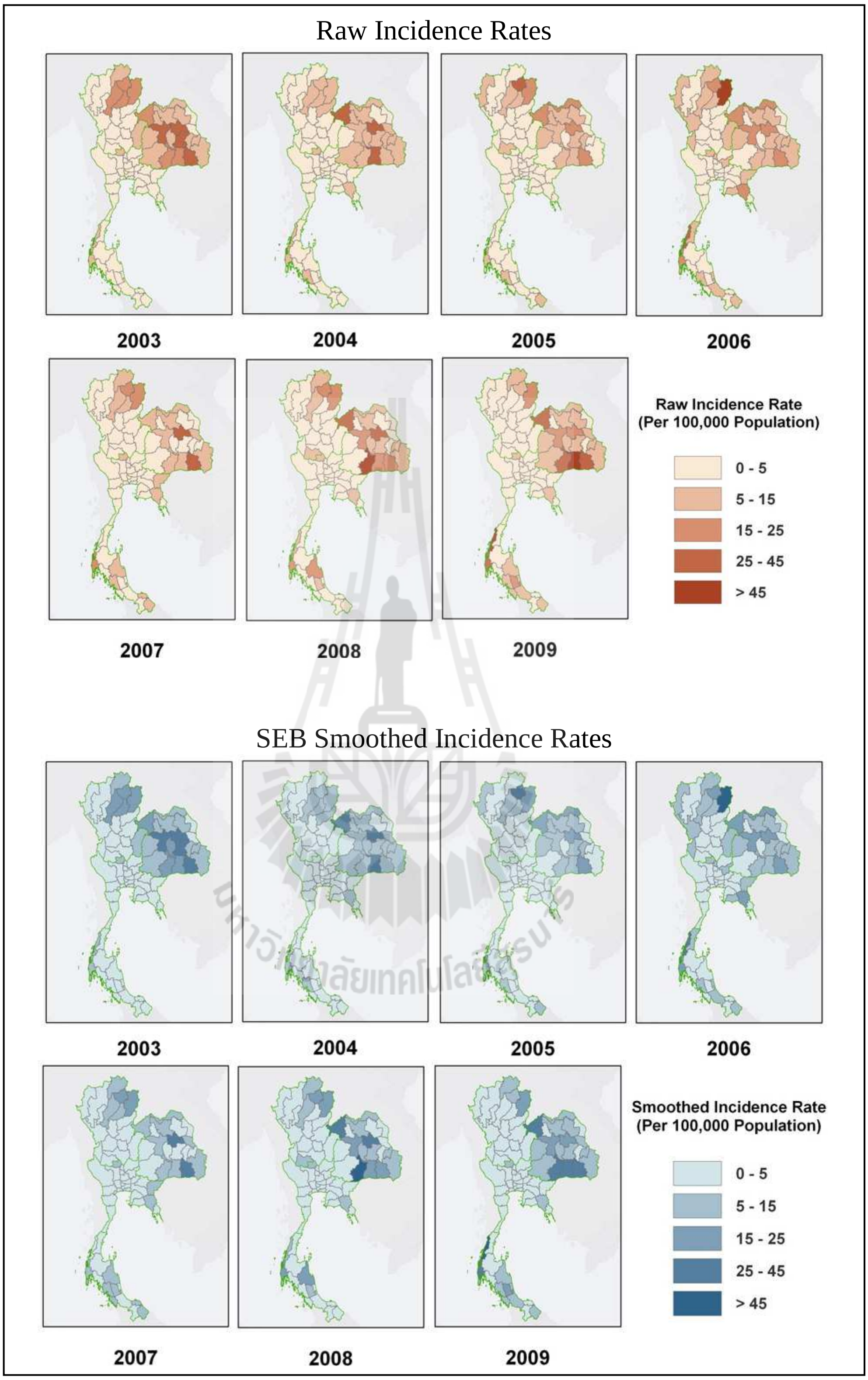


Figure 4.6 Comparison of raw and SEB smoothed incidence rates of leptospirosis by province, 2003-2009.

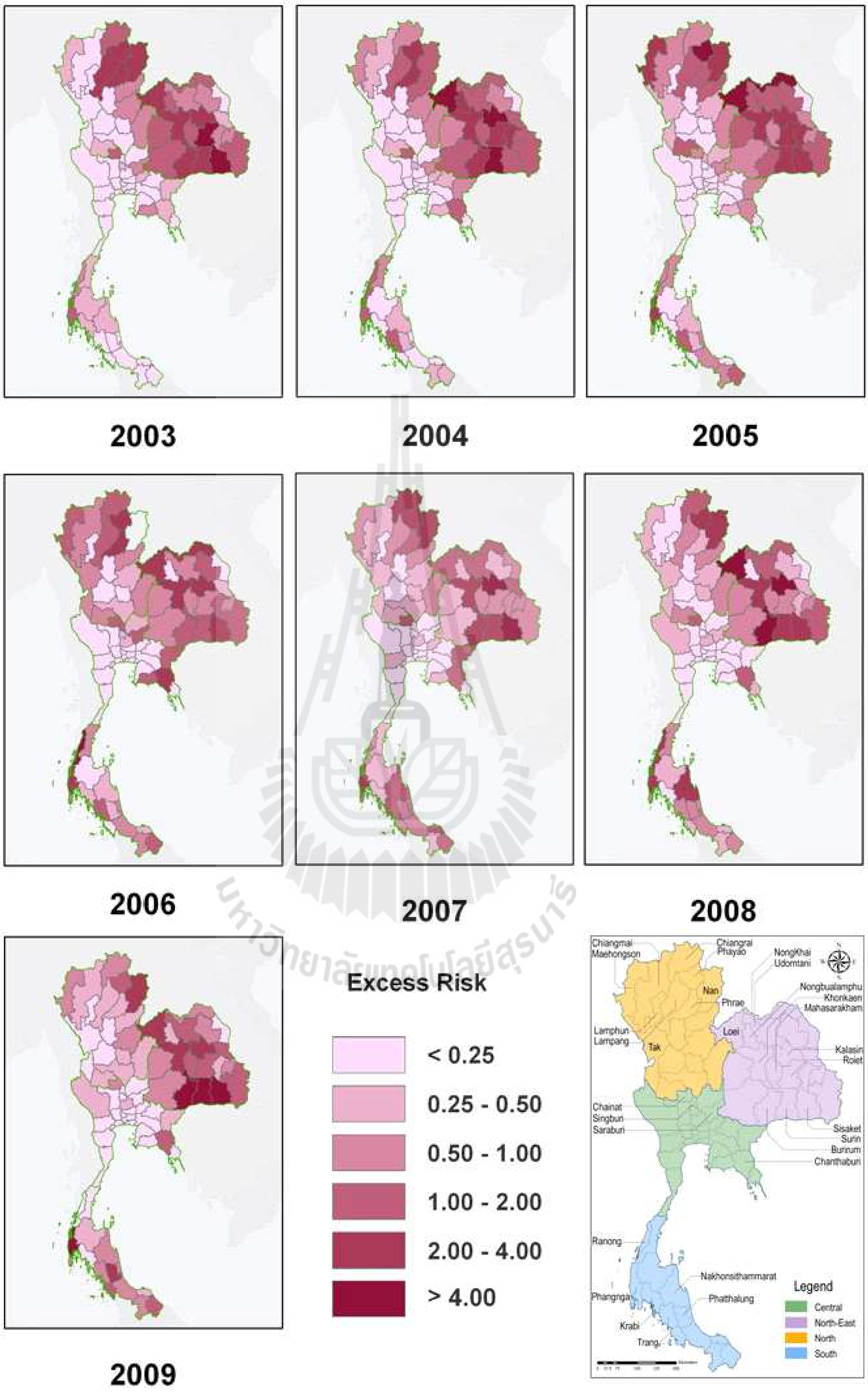


Figure 4.7 Excess risks of leptospirosis by province, 2003-2009.

Excess risk map was produced to facilitating the one who want to know how many times the risk of being a leptospirosis case in each province as compare to overall average risk calculated from data of entire Thailand. These maps were portrayed in Figure 4.7. Provinces with excess risk of greater than 1 were those with higher risks than the overall risk. On the other hand, provinces with excess risk of less than 1 were the lower risk provinces. For every year, the higher risks were observed in most of northeastern provinces and some northern provinces. A few provinces in southern Thailand, Ranong and Phang Nga, got high risk almost every year. The details of excess risks by province in the separated years from 2003 to 2009 were presented in Appendix A.

4.1.2 Spatial, temporal and spatio-temporal clusters of leptospirosis

4.1.2.1 Spatial clusters

Seven significant spatial clusters of leptospirosis were detected by purely spatial analysis. Figure 4.8 demonstrated the distribution of these spatial clusters. The most likely cluster was in four provinces of northeast region, i.e., Burirum, Surin, Sisaket, and Roi Et (province code: 31, 32, 33, 45). The second and the third clusters were also in northeast region while cluster 4 to 7 cluster were in other region.

Table 4.3 showed details of each significant spatial cluster. It pronounced the number of province(s) in each cluster, as well as number of population, numbers of observed and expected cases, relative risk, and p-values. The relative risk showed how many times the observed incidence rate was higher than the expected rate in each cluster. There were 8,154 leptospirosis cases out of 5,678,662 population occurred in the first cluster. The relative risk of this cluster was 4.18. This means that the incidence rate in this cluster was 4.18 times more than the expectation.

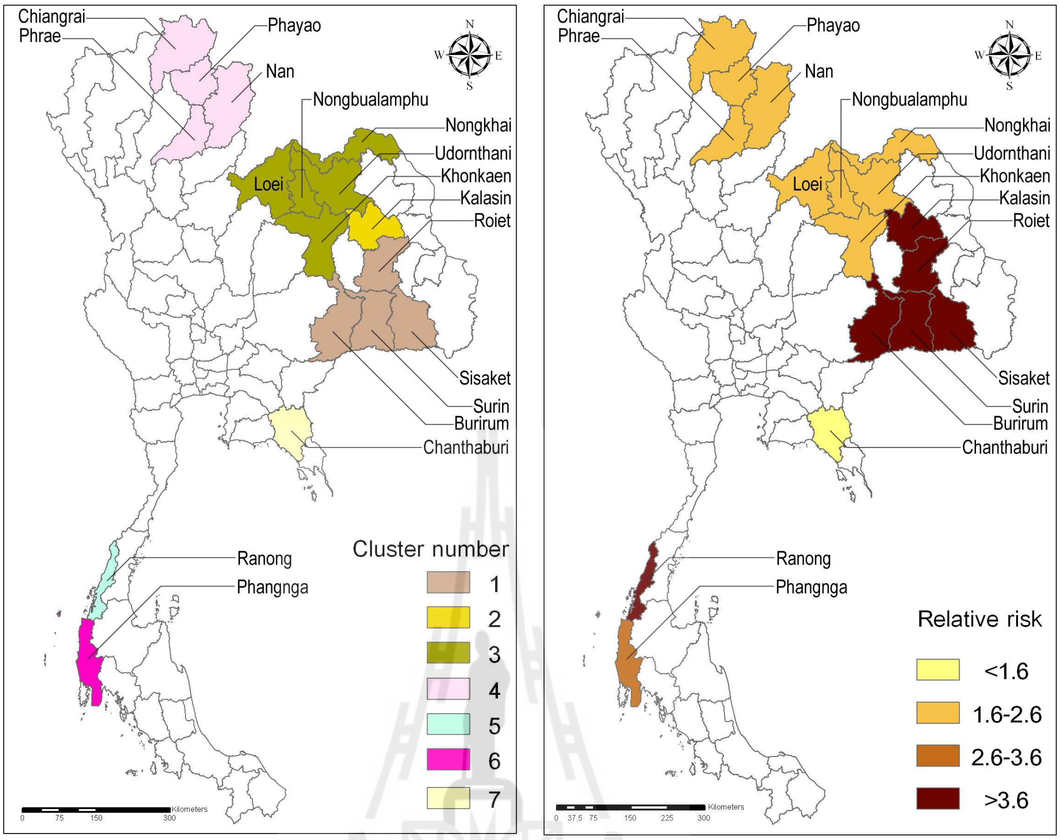


Figure 4.8 Maps of significant spatial clusters during 2003-2009.

Table 4.3 Detail characteristics of purely spatial clusters.

No.	**Province**	**Population**	**Observed Cases**	**Expected Cases**	**Relative Risk**	**P-Value**
1	Burirum, Surin, Sisaket, Roi Et	5,678,662	8,154	2,512.12	4.18	<0.001
2	Kalasin	979,213	1,969	433.18	4.82	<0.001
3	Nong Bua Lamphu, Udon Thani, Loei, Khon Kaen, Nong Khai	5,302,374	5,098	2,345.66	2.44	<0.001
4	Phayao, Chiang Rai, Phrae, Nan	2,667,056	2,321	1,179.85	2.01	<0.001
5	Phangnga	243,915	299	107.90	2.79	<0.001
6	Ranong	176,263	341	77.97	4.42	<0.001
7	Chanthaburi	503,482	337	222.73	1.52	<0.001

4.1.2.2 Temporal cluster

There was only one significant temporal cluster of leptospirosis occurred during July to November 2009. This denoted that there only was one significant temporal cluster of months with high leptospirosis without considering the places where the cases were infected. The outputs were shown in Table 4.4 and Figure 4.9 and revealed that there were 3,649 cases observed in this temporal cluster while its expectation was only 1,678 cases. The incidence rate was 2.35 times higher than the expected one.

Table 4.4 Detail characteristic of purely temporal cluster.

Cluster No.	Time Period	Annual Cases per 100,000	Observed Cases	Expected Cases	Relative Risk	P- value
1	Jul–Nov 2009	13.7	3,649	1,677.93	2.35	<0.001

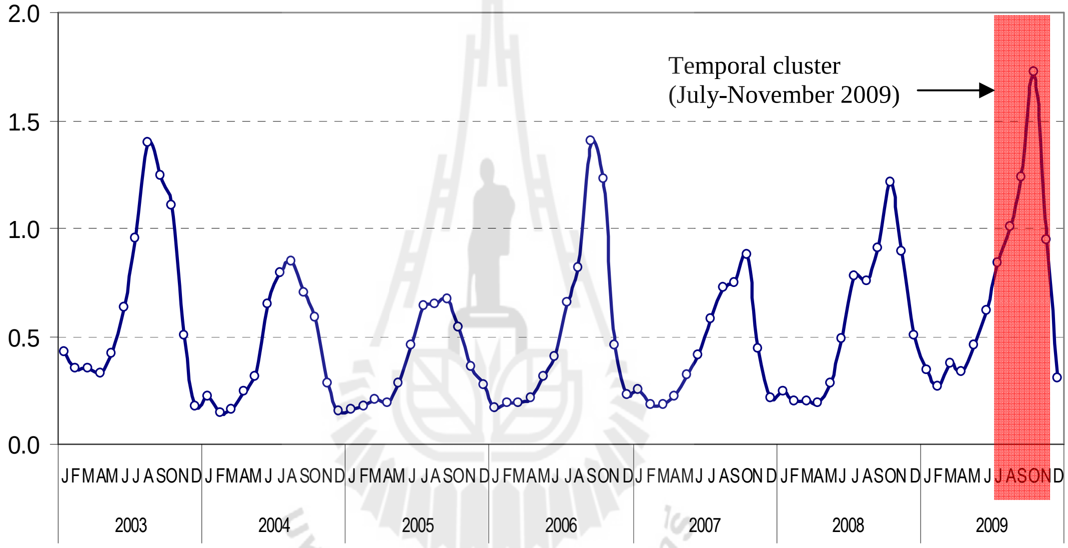


Figure 4.9 Monthly incidence rates of leptospirosis in Thailand with a significant temporal cluster.

4.1.2.3 Spatio-temporal cluster

There were eleven space-time clusters significantly occurred in Thailand during 2003-2009 (Figure 4.10 and Table 4.5). Three of them (Cluster 1, 2, 6 in Table 4.4) were in northeast region with quite high relative risks of 13.3, 6.9 and 7.4, respectively. The first cluster composed of 3 provinces in northeast region, i.e., Burirum, Surin and Sisaket which had occurred during July to November 2009. More than 1400 cases of leptospirosis were observed in this cluster, while the expected cases were calculated only 115.3 cases. The second cluster in northeast region comprised 4 provinces, i.e., Khon Kaen, Mahasarakham, Roi Et and Kalasin which had occurred between July and October 2003. The observed cases were 1,019 cases and the expected cases were 133. Another one cluster included Loei and Nong Bua Lamphu in between July and October 2004. Even the observed cases in this cluster were 187 cases which were very few as compared to the former clusters, the expected cases in this area were only 29.5. It built relative risk high enough to be a significant cluster.

The remaining clusters were scattered in other regions, i.e., 3 clusters in the north, 3 clusters in central region and 2 clusters in the south. The reports from flooding database of **HAII - Hydro and Agro Informatics Institute** (www.haii,or.th or www.thaiwater.net) were used for the additional explanation of each space-time clusters. Each individual cluster was compared to HAII flood incidence records. Five space-time clusters were related to the place and time of flood incidence recorded in HAII database, while the rest six clusters were not. All 3 space-time clusters in northeast region did not coincide with flood. The clusters which occurred coincident with flood were cluster 3 (Nan), 4 (Ranong), 8 (Nakhon Sri Thammarat, Krabi, Phangnga, Phuket, Trang, Phatthalung), 10 (Sing Buri and Chai Nat) and 11 (Tak). The selected flood events which occurred coincided with these spatio-temporal clusters were shown in Table 4.6.

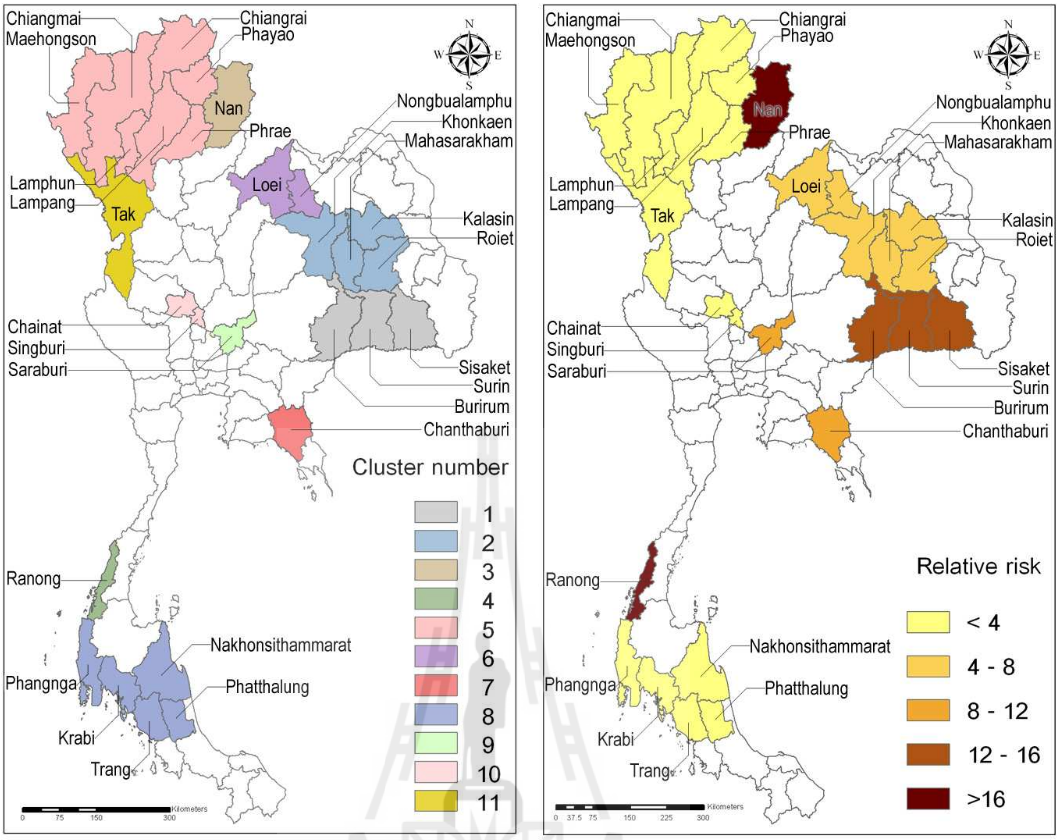


Figure 4.10 Maps of significant spatio-temporal clusters during 2003-2009.

Cluster 3 (Nan) and cluster 4 (Ranong) were very high relative risks (56.5 and 37.5, respectively). Relative risks of the remaining 3 clusters (cluster 8, 10, 11) were not so high but they exhibited the statistically significant. These results might draw the conclusion that flooding disaster in the northeast region did not show the outstanding amplification of leptospirosis transmission, while flooding in other region might trigger leptospirosis transmission. In addition, the flooding database of HAII documented that the well-known typhoon ‘Sang San’ was occurred in September 2006. It devastated wide areas included areas in Nan, Sing Buri, Chai Nat and Tak. This might be a reason why cluster 3, 10 and 11 were significantly occurred during that time.

Table 4.5 Detail characteristics of spatio-temporal clusters.

No.	Province	Time	Population	Observed Cases	Expected Cases	Relative Risk	P-value
1	Burirum, Surin, Sisaket	Jul-Nov 2009	4,366,537	1,462	115.37	13.32	<0.001
2	Khon Kaen, Maha Sarakhom, Roi Et, Kalasin	Jun-Oct 2003	4,983,818	1,019	132.97	7.92	<0.001
3	Nan	Aug-Sep 2006	478,716	282	5.04	56.48	<0.001
4	Ranong	Jun-Nov 2009	176,263	215	5.79	37.48	<0.001
5	Chaing Mai, Lamphun, Lamphang, Phrae, Phayao, Chiang Rai, Mae Hong Son	Jul-Oct 2003	5,265,975	385	112.20	3.47	<0.001
6	Loei, Nong Bua Lam Phu	Jul-Oct 2004	1,114,819	187	29.48	6.38	<0.001
7	Chanthaburi	Sep-Nov 2006	503,482	85	7.89	10.81	<0.001
8	Nakhon Sri Thammarat, Krabi, Phangnga, Phuket, Trang, Phatthalung	Jun-Nov 2009	3,564,546	266	114.89	2.33	<0.001
9	Saraburi	Oct 2009	612,787	27	3.26	8.30	<0.001
10	Sing Buri, Chai Nat	Jul-Oct 2006	559,418	39	11.85	3.29	<0.001
11	Tak	Jul-Oct 2006	522,153	32	11.18	2.86	0.026

Table 4.6 Summary of flood events which occurred coincided with some spatio-temporal clusters.

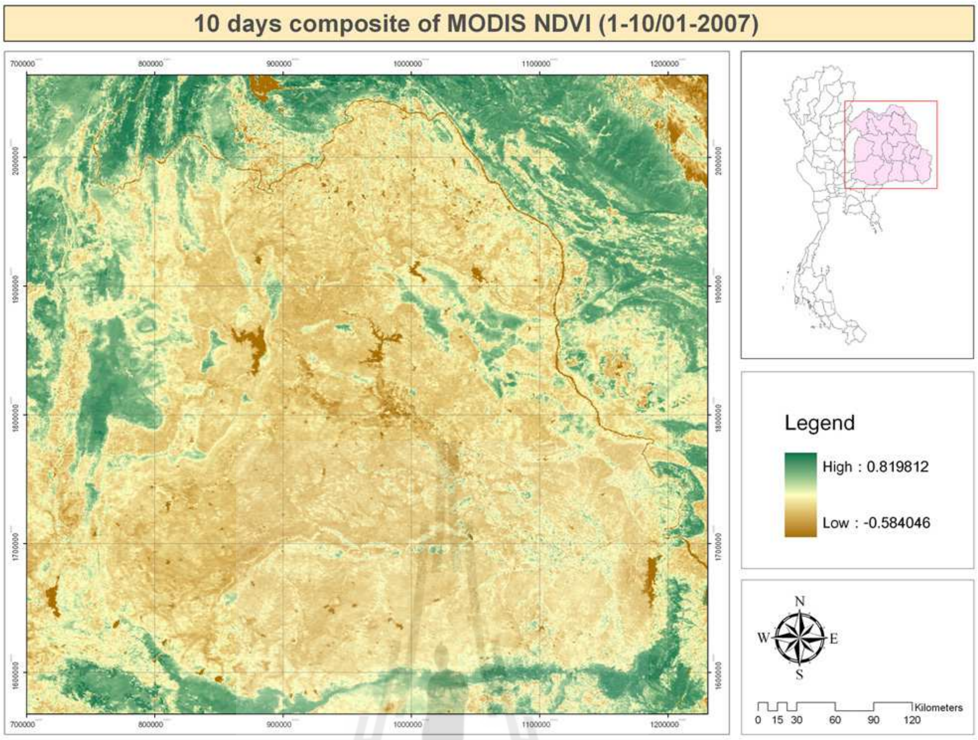
Month-Year	Affected Region	Affected Province
Aug-Sep 2006	North	Nan, Payao, Chieng Rai
Sep-Oct 2006	Central	Chai Nat, Sing Buri, Suphan Buri, Ang Thong
	North	Tak, Sukhothai
Jul 2009	South	Ranong, Satun, Trang, Phang Nga
Nov 2009	South	Nakhon Sri Thammarat, Trang, Phatthalung, Songkhla

4.1.3 Spatial variations of the relationships among predictor variables and leptospirosis in northeast region

4.1.3.1 MODIS data processing

Since leptospiral bacteria survive in water and mud or moist soil condition, the temporal variation of the areas with such condition must be investigated for the evaluation of possible relationships to the incidence of leptospirosis. Amount of inundated areas, therefore, was set as a main factor of interest of this research. MODIS data were selected due to its high temporal resolution could serve the needs of this research.

Cloud-free 10-day composite MODIS images over the northeast region of Thailand in 2007 were processed by methods described above. Series of 36 NDVI images and 36 LSWI images were produced. Thirty-six images of inundated areas (3 images per month) were obtained after analyzing by using the proposed algorithm. The example images of NDVI, LSWI and inundated areas were demonstrated in Figures 4.11 to 4.13.



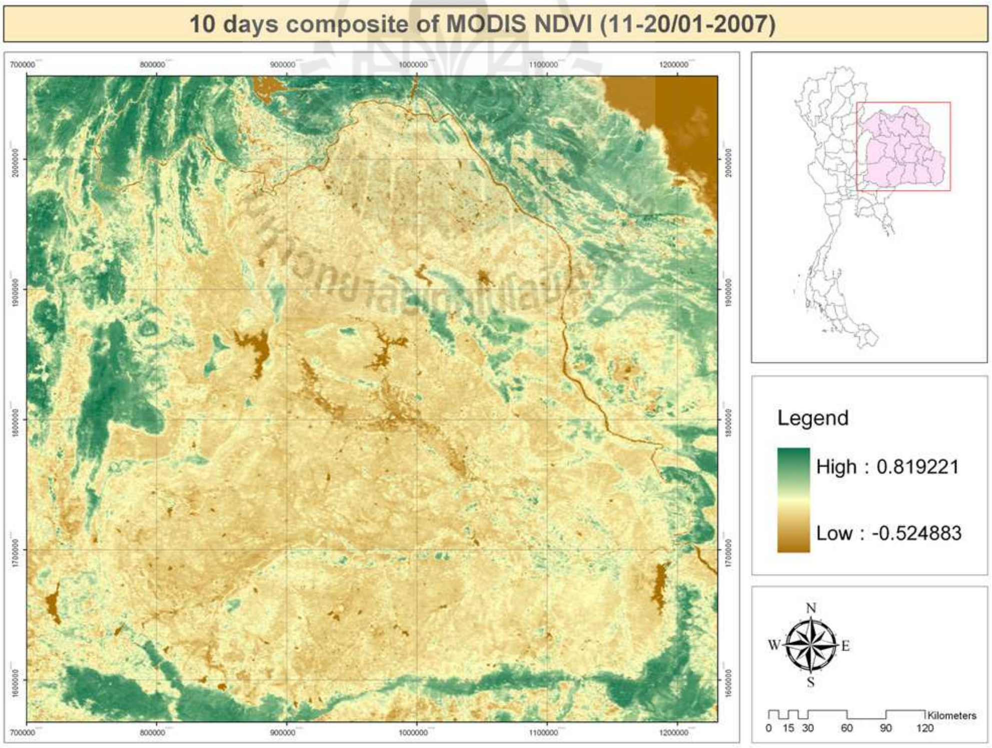


Figure 4.11 Example of 2 images of NDVI over northeast region.

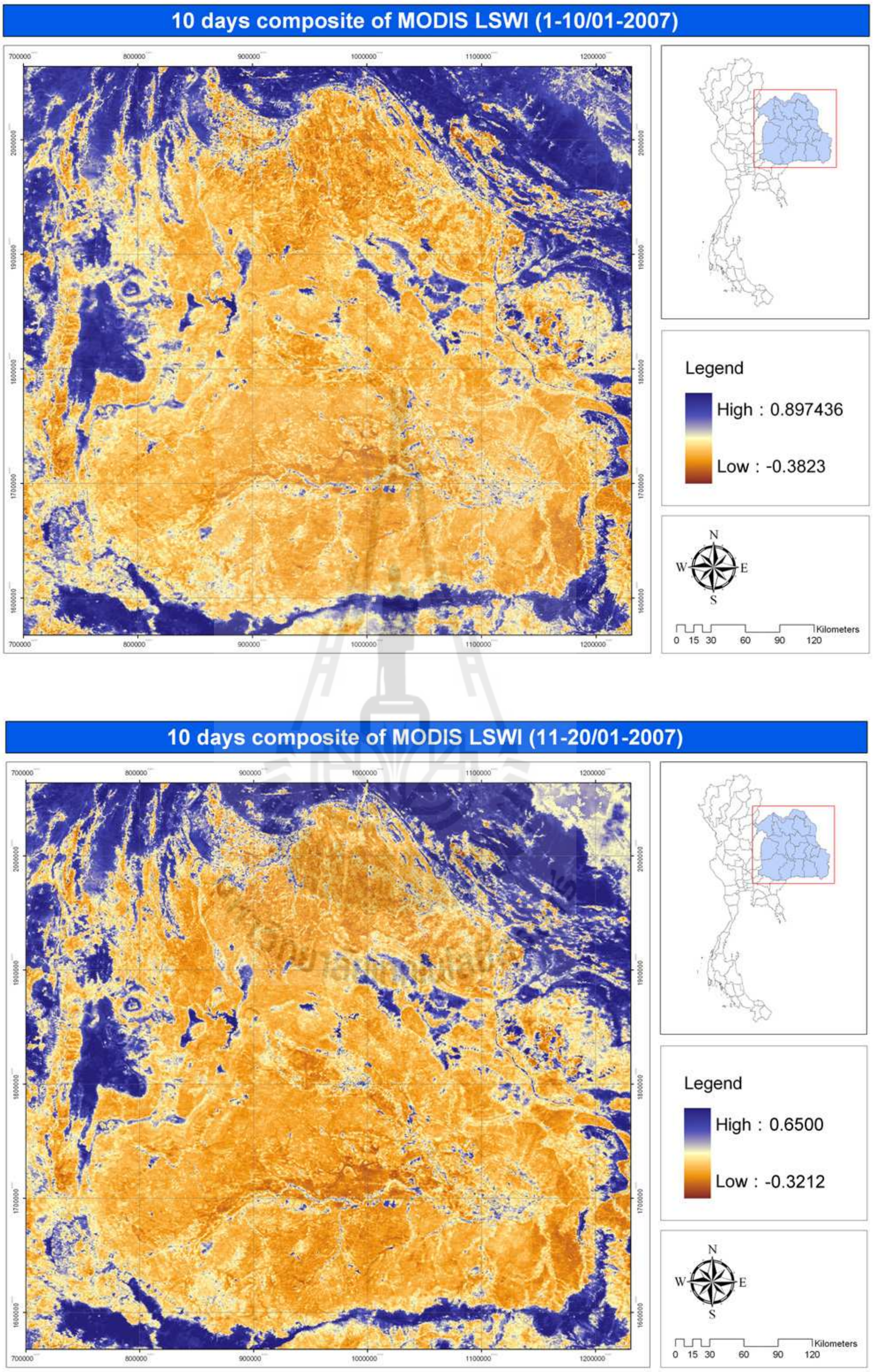


Figure 4.12 Example of 2 images of LSWI over northeast region.

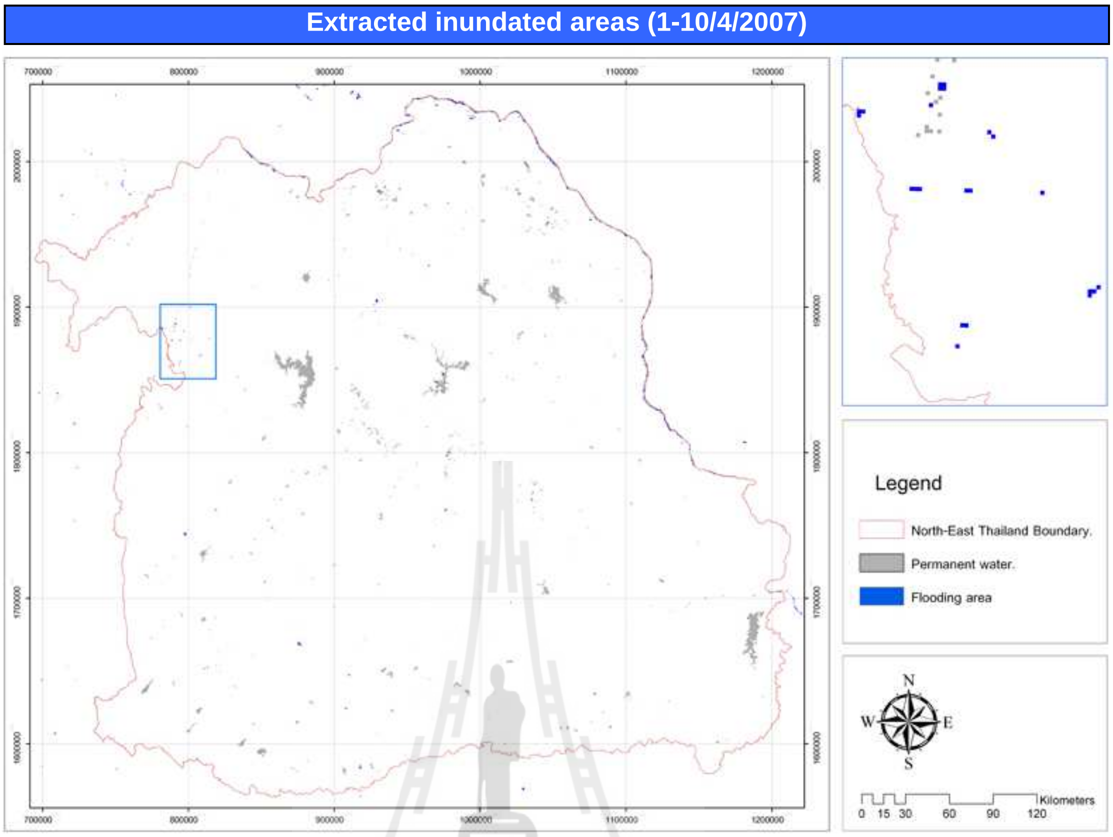


Figure 4.13 Example of an image inundated areas of extracted from MODIS data.

Provincial boundary map was overlaid on each image of inundation to summarize the quantities of inundated areas of each province (in square kilometers) by using zonal operation function in ArcGIS software. Finally, monthly average of inundation areas for each province was calculated and the result was shown in Table 4.7.

The assessment of the accuracy of MODIS image classifications was done prior to using the output as an independent variable in further analysis. The overall accuracy was 92.2 percent while agreement in the classification of inundated area is good (Kappa=0.74). The detail of the assessment results were demonstrated in Appendix B.

Table 4.7 Inundated areas (sq km) in northeast region in 2007 extracted from MODIS images.

Code	Province	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec
30	Nakhom Ratchasima	22.1	32.4	11.8	3.6	275.0	177.9	72.7	166.8	261.0	192.4	31.1	37.8
31	Burirum	16.0	12.2	6.9	3.8	179.8	227.9	57.3	68.1	78.8	59.7	28.4	20.8
32	Surin	4.2	2.3	0.4	1.5	24.8	8.4	20.8	31.0	41.2	133.4	13.4	5.5
33	Sisaket	4.8	6.3	2.9	3.2	29.4	17.4	52.1	79.8	107.6	73.3	13.9	4.8
34	Ubon Ratchathanee	12.4	12.0	4.6	5.7	17.9	162.0	90.3	127.0	163.6	146.4	38.2	14.9
35	Yasothon	0.6	1.3	0.0	0.0	4.4	4.8	0.0	38.5	77.1	32.1	5.0	1.7
36	Chaiyaphu	3.2	6.1	5.7	2.5	18.3	25.2	460.1	289.4	118.7	24.6	12.6	10.1
37	Amnat Chareon	4.0	4.6	2.9	2.9	4.8	44.7	31.9	44.0	56.1	9.5	6.1	5.7
39	Nong Bua Lamphu	0.4	0.4	0.0	0.8	0.0	0.8	12.6	7.2	1.9	15.3	2.5	2.1
40	Khonkaen	9.0	6.5	2.5	0.8	3.2	7.6	80.0	60.4	40.8	51.3	17.0	10.1
41	Udon Thanee	6.9	5.5	4.4	3.8	1.3	21.6	83.0	76.4	69.7	43.5	19.7	11.6
42	Loei	6.3	2.7	2.7	7.1	14.1	19.1	306.3	163.6	21.0	16.8	15.3	6.9
43	Nong Khai	40.1	44.5	41.0	42.0	60.9	108.6	129.4	200.0	270.6	147.3	109.9	96.0
44	Maha Sarakham	11.1	4.8	1.7	1.9	4.8	18.7	0.8	13.3	25.8	29.4	13.2	9.7
45	Roi Et	5.0	3.2	0.4	0.6	7.1	21.8	0.6	47.2	93.7	97.1	28.1	7.6
46	Kalasin	13.4	11.1	2.1	2.5	2.7	24.4	8.6	32.2	55.9	85.5	29.0	18.9
47	Sakon Nakhorn	8.2	6.7	3.2	3.2	9.7	99.8	127.3	162.1	196.8	22.3	12.0	14.9
48	Nakhon Phanom	39.3	43.7	19.5	16.0	44.3	142.8	66.2	151.6	237.0	79.8	54.6	57.6
49	Mukdahan	11.8	17.9	8.2	16.0	13.4	67.6	26.7	25.0	23.3	32.1	17.0	20.2
All provinces		**219**	**224**	**121**	**118**	**716**	**1201**	**1627**	**1783**	**1940**	**1292**	**467**	**357**

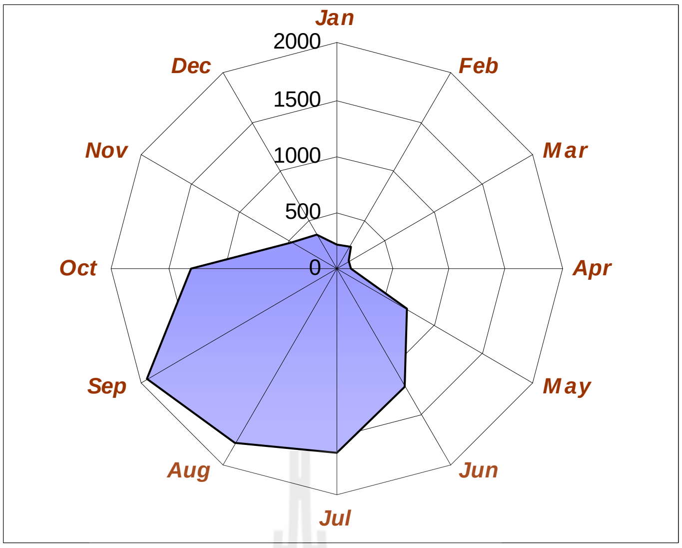


Figure 4.14 Monthly variation of inundated areas in northeast region in 2007.

Figure 4.14 illustrates monthly variation of inundated areas in northeast region in 2007. Inundation areas were small during the first 4 months (January-April) and then increasing month by month from May to reach the highest in September. The flooded areas were abruptly decreasing in October and continuing until December. This information supported the results from temporal and spatio-temporal cluster analyses. Temporal distribution of leptospirosis was in the months with high inundation areas. The data of inundated areas in Table 4.7 were used as major independent variable in regression analyses.

4.1.3.2 Global and local regression analyses

Before performing regression analysis, each independent variable was explored for the normality of the distribution. Two variables, i.e., **Inundated areas** and **Rainfall** were skewed. Therefore, logarithmic transformations were applied to those variables (Figure 4.15). The logarithmic values of these two variables were used instead of the original ones throughout the analyses. The list of independent variables used for regression analyses was presented in Table 4.8.

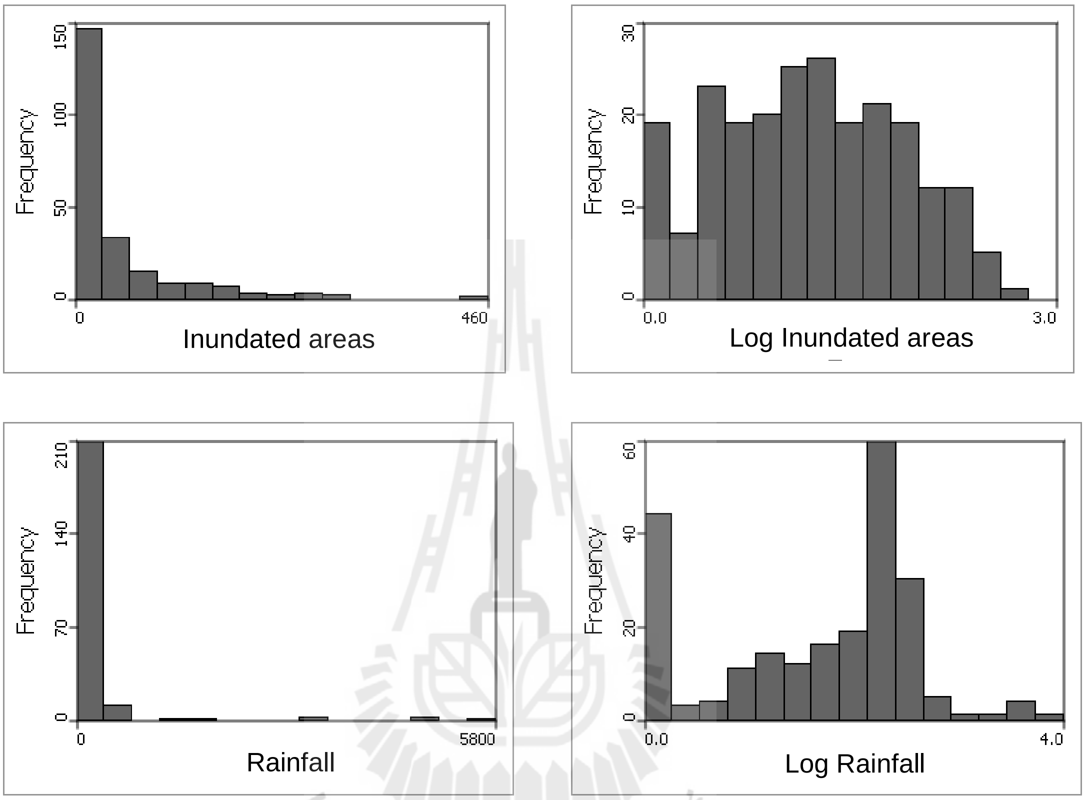


Figure 4.15 Histograms of skewed variables and their logarithmic transformations.

Table 4.8 Independent variables used in regression models.

Variable Name	Description
LogInundat	Logarithm of inundated areas extracted from MODIS (km^2)
LogRain	Logarithm of monthly rainfall (mm)
RainyDay	Number of rainy days in a month
Paddy	Rice paddy areas (km^2)
AquaCult	Aquaculture areas (km^2)
Livestock	Livestock farming areas (km^2)
AgriDen	Agriculture population density (persons/km^2)

All independent variables were put into the global Poisson regression model and let the program find the best model. Table 4.9 showed the summary of model selection. The best model was the model with highest value of Log Likelihood and comprised all of the seven variables. The parameter estimates (intercept and regression coefficients), standard errors and p-values were presented in Table 4.10. The parameter estimates of all variables were highly significant with very small p-values.

Table 4.9 Summary of global Poisson regression model.

Best Subset Summary:

Terms	Log likelihood
AgriDen AquaCult LogRain LogInundat Livestock Paddy RainyDay	4.593E 9
AgriDen LogRain LogInundat Livestock Paddy RainyDay	4.583E 9
AgriDen AquaCult LogRain Livestock Paddy RainyDay	4.566E 9
AgriDen AquaCult LogRain LogInundat Paddy RainyDay	4.565E 9
AgriDen LogRain LogInundat Paddy RainyDay	4.562E 9
AgriDen LogRain Livestock Paddy RainyDay	4.558E 9
AgriDen AquaCult LogRain Paddy RainyDay	4.546E 9
AgriDen LogRain Paddy RainyDay	4.544E 9
AquaCult LogRain LogInundat Livestock Paddy RainyDay	4.542E 9
AgriDen AquaCult LogRain LogInundat Livestock Paddy	4.539E 9

Goodness of Fit:

DF	Deviance	Deviance/DF
220	2.299E 9	10450402
LogLikelihood	4.593E 9	

Table 4.10 Parameter estimates of the final global Poisson regression model.

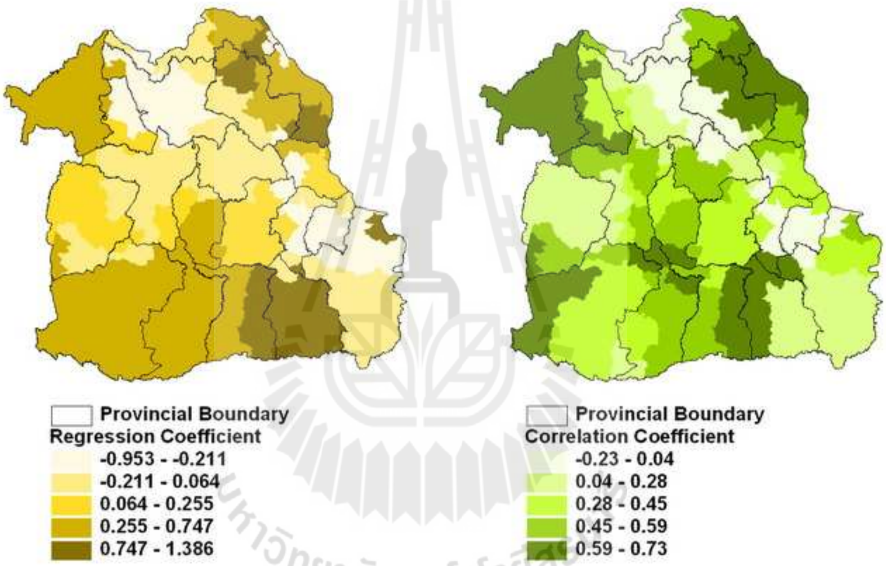
Term	D.F.	Parameter est.	Std error	P value
Intercept	1	-0.57164	0.000173	0.0
AgriDen	1	0.00586	0.585E-6	0.0
AquaCult	1	0.007313	0.000002	0.0
LogRain	1	0.282194	0.000026	0.0
LogInundat	1	0.25167	0.000035	0.0
Livestock	1	-0.00652	0.883E-6	0.0
Paddy	1	0.000322	0.205E-7	0.0
RainyDay	1	0.029022	0.000003	0.0

The software also generated the regression residual (error term in the regression equation) at each location in space. The residuals were test for autocorrelation using Univariate Local Moran Method as a test statistic. The test result shown in Table 4.11 revealed that local Moran's I equal to 0.602 with the p-value of 0.001. This means there was spatial autocorrelation of residuals in some locations in space. It indicated that the spatial process of leptospirosis in northeast region appeared to be non-stationary over the area. Therefore, Global Poisson regression model obtained earlier could not be used for the explanation of relationships of those variables to leptospirosis incidence rates. Subsequently, the spatial non-stationarity process was assumed and local regression model must be used as an alternative.

Table 4.11 Output result of the test for autocorrelation of the residuals.

Univariate Local Moran method		
Number of randomizations = 999 Spatial weights set = Nearest 5 neighbors Alpha level = 0.05 Use Simes correction = Yes		
Moran's I	=	0.602089
P value	=	0.001000

The local regression used in this study was GWPR. The GWPR analysis was performed by the same software. All seven independent variables shown in Table 4.8 were put into the model. The result revealed that only four variables were significantly fitted to the model. These predictor variables were:- **inundated areas; agriculture population density**; **rainfall**; and **number of rainy days**. The model parameter estimates (intercept and regression coefficients) of those four variables at every regression points (district centroids) were obtained. The program also calculated the correlation coefficient, r, between each predictor variable and leptospirosis incidence at each location. These correlation coefficients were also mappable. The Choropleth maps of local parameter estimates (regression coefficients) and correlation coefficient in Figure 4.16 to Figure 4.19 depict the variations in the relationships between the incidence of leptospirosis and each predictor variable.

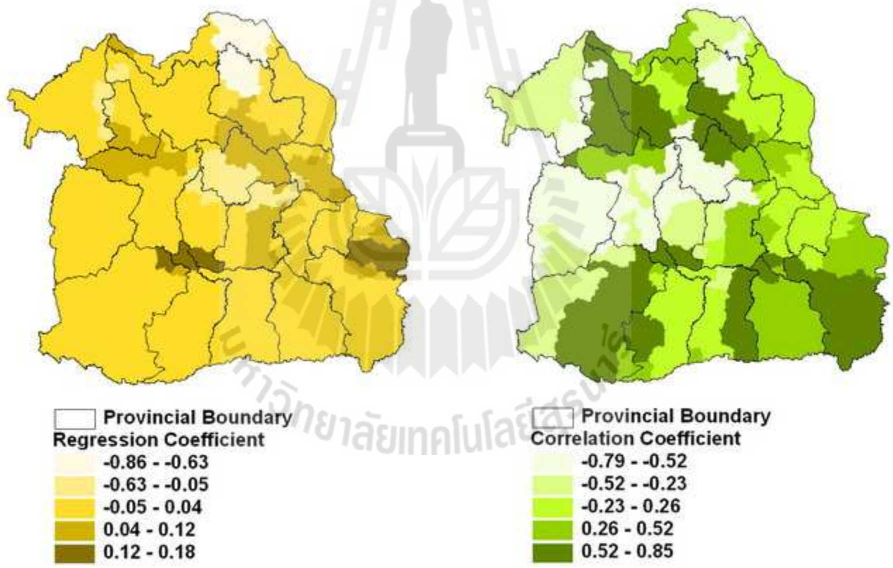


(*a*) (*b*)

Figure 4.16 Choropleth maps of (*a*) parameter estimates of inundated area, and (*b*) correlation coefficients.

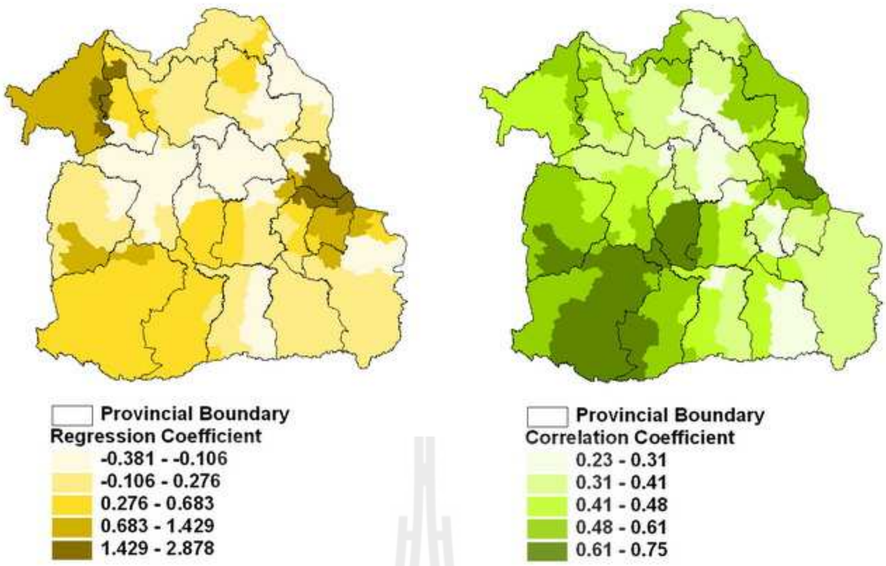
In Figure 4.16 (*a*), the influence of "inundated areas" on leptospirosis incidence rates varied substantially over the region. Some locations were much affected and some were less. The highest affected areas were some districts in the lower right part and a few districts in the upper right part of the region. The correlation of inundated areas and leptospirosis incidence rates in Figure 4.16 (*b*) portrayed the same pattern as of the regression coefficients.

"Agriculture population density" was also a significant predictor in the final model. The areas with high regression coefficients in Figure 4.17 (*a*) appeared at some areas of Ubon Ratchathani, Khon Kaen and Mahasarakham province. Leptospirosis incidence rates in other areas seem to be less affected by this predictor. The clusters of high correlation coefficients (Figure 4.17 (*b*)) differed from the pattern of regression coefficients. The correlation between this predictor and leptospirosis was high in those clusters, but the influence of predictor on the leptospirosis occurrence was less.



(*a*) (*b*)

Figure 4.17 Choropleth maps of (*a*) parameter estimates of agriculture population density, and (*b*) correlation coefficients.

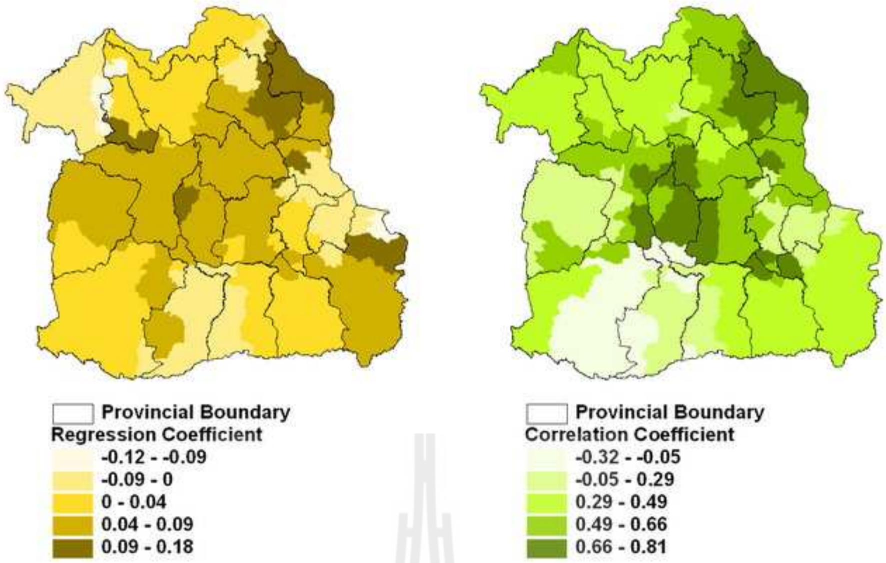


(*a*) (*b*)

Figure 4.18 Choropleth maps of (*a*) parameter estimates of amount of rainfall and (*b*) correlation coefficients.

Effect of "Rainfall" on leptospirosis incidence rates was pronounced in some areas in the upper and lower parts of the region as shown in Figure 4.18 (*a*). Amount of rainfalls were likely to exhibit less effect in the middle part of the region. The distribution of high correlations (Figure 4.18 (*b*)) was in the same pattern.

The dispersion of regression coefficients of "Rainy days" in Figure 4.19 (*a*) were clustered in some areas in the upper part of the region. Other areas were less influenced by rainy days. Figure 4.19 (*b*) depicts the variation of correlation between number of rainy days and incidence rates of leptospirosis. The pattern was not much different from the regression pattern.



(*a*) (*b*)

Figure 4.19 Choropleth maps of (*a*) parameter estimates of number of rainy days, and (*b*) correlation coefficients.

4.2 Discussion

This research has demonstrated the use of geoinformatics and spatial statistics in a spatial epidemiological study of leptospirosis in Thailand with the emphasis on the northeast region. General results of this study supported the evidence that leptospirosis is a burdensome disease of human health in Thailand which is the same as other countries in the tropics where the appropriate environmental conditions for survivals of infective agents are available in the countries. In some developed countries, unlike Thailand, leptospirosis is a disease of economics significance in animal husbandry (Levett, 2001) rather than human illness.

The spatial patterns of leptospirosis by region of Thailand were obtained from this study. Table 4.1 and Figure 4.1 generally showed that northeast region was experiencing the highest incidence of leptospirosis throughout the study period.

Figures 4.4 and 4.5 supported more scientific results and proved that leptospirosis incidences in many provinces of northeast region were very high.

Monthly leptospirosis incidence rates in Thailand during 2003 and 2009 shown in Figure 4.2 revealed the obvious seasonal pattern with the peak between August and October in the late rainy season every year. The same temporal patterns were observed in other countries in Southeast Asia due to a wider environmental contamination during the wet season (Riccardo and Bayugo, n.d.).

Recently, the issue of climate change and global warming has been raised up for discussion in various forums worldwide. The changing climate may affect environmental conditions that lead to the changes of leptospirosis transmissions in either positive or negative directions in different locations. The way this research did can be used in the study of such changes. First of all, the ESDA should be done to discover the true distribution of the disease. This research used the smoothed rates for the comparison of incidence across the study area. The map of smoothed rates presented in Figure 4.4 was capable in the comparison of the extent of leptospirosis transmission among different provinces and different units of time Moreover, the excess risk map in Figure 4.5 displayed how many times the risk of each province more or less than the overall average risk in Thailand. From such maps, it is interesting that some provinces in the south were at high risk but surrounded by low-risk provinces. The high-risk provinces might have some specific factors that facilitated the transmission of leptospirosis. More detail studies are required to explain such occurrence. These mapping results can be a raw material for the initiation of further studies or further interventions. They can be the useful tools for health policy makers too.

The results in section 4.1.2 reveal that there were significant spatial clusters, temporal cluster and spatio-temporal clusters at the provincial scale in Thailand. These results prove that the first study hypothesis was true. The purely spatial clusters shown in section 4.1.2.1 express the heterogeneity of leptospirosis occurrence in Thailand provinces. Not all provinces had the similar transmission of leptospirosis during the study period. Three spatial clusters in northeast region (comprising 10 provinces) were declared.

Most of leptospirosis cases in Thailand occurred in association to the agricultural environment and flooding in some areas (Kaewpa, 2002; Tangkanakul et al., 2000; Tangkanakul et al., 2005). It was also similar to leptospirosis situations in Southeast Asia as reviewed by Riccardo and Bayugo (n.d.) that climatic and environmental conditions, population density and behavioral factors favored the transmission of the disease in the Region. Results of this study were slightly the same and the significant factors associated to leptospirosis were inundation areas, population density and number of rainy days. In Brazil, leptospirosis occurred more in urban than rural area, unlike Thailand, but the risk factors were rather similar as such the occasional flooded areas was an important factor in disease transmission (Barcellos and Sabroza, 2001; Correia et al., 2004).

The results supported that there were significant variations of the relationships among the predictor variables (inundated areas, population density and number of rainy days) and the incidence of leptospirosis across the region. Therefore, spatial non-stationarity was assumed. In spatial non-stationary process, the same factor causes a different response in different parts of the study region. The same amount of inundation areas caused a dissimilar leptospirosis incidence in difference provinces.

The actions of “population density” and “number of rainy days” were also the same as the “inundated areas” did. If this non-stationarity process is modeled by stationary models, a wrong conclusion might be drawn.

The output results of parameter estimates might be bias due to the modifiable areal unit problem (MAUP). MAUP is the challenge that occurs during the analysis of aggregated data in which the results differ when the same analysis is applied to the same data but using different aggregation scheme. The data used in this study were aggregated to the provincial unit. The results would differ from the results that analyzed from the smaller aggregated unit, such as district unit. This is a constraint of this study that only province-aggregated data were obtained under the limited resources. Nevertheless, this study tried to interpolate the parameter estimates to the district unit in the local regression analysis by using province centroids as the data points and employed the district centroids as the regression points. The results might not be as accurate as those drawn from the analysis of district-aggregated data themselves.

CHAPTER V

CONCLUSION AND RECOMMENDATIONS

5.1 Conclusion

Although the etiology and epidemiology of leptospirosis have been understood for many years and such understanding has led to the development of helpful prevention and control measures, more knowledge on spatial and temporal pattern of each specific and confined area is still required in order to use for launching most appropriate measure to the specific place. This retrospective research attempted to study the spatial and temporal epidemiology of leptospirosis and uncover the possible factors that related to disease dispersion.

The study was designed to emphasize to the northeast region because of its higher incidence than other regions. Result from descriptive part of the research also demonstrated the dense distribution in northeast region. The output disease maps have facilitated knowledge on geographical distribution of leptospirosis at the provincial scale. Moreover, the maps of significant clusters of disease were produced. They indicated the areas of higher incidence and also provided valuable information on spatial pattern and temporal change of the disease incidences. Such maps have clear advantages over the tables from classical researches which did not consider the spatial aspects.

Cluster analysis using scan statistics can be used without the need of prior test for global clustering. Scan statistics can also be effectively used to scan for purely spatial clusters or purely temporal clusters or spatio-temporal clusters. Location of cluster can be ultimately obtained if the significant cluster was available. The study results reveal that there were seven spatial clusters, one temporal cluster and eleven spatio-temporal clusters occurred in northeast region during 2003 and 2009. The output maps can show the disease hot spot and may be used to identify the prominent risk areas for leptospirosis infection in Thailand. Consequently, they can help highlighting the need for intervention or for further investigation.

The emphasizing analysis for spatial relationship between leptospirosis incidence rates and environmental factors was performed to the data of northeast region between January and December 2007. The remotely-sensed data from MODIS on-board the Terra Satellites were used to extract the inundated areas, the suspecting factor that contributed leptospirosis transmission.

The results of this research also demonstrated the variations in spatial relationships among environmental factors and leptospirosis incidences in northeast region. Four significant factors were demonstrated from the local regression, GWPR model. These variables were: i) amount of actual inundated areas, ii) agricultural population density, iii) amount of monthly rainfalls and iv) number of rainy days in a month. The parameter estimates (regression coefficients) as well as correlation coefficients of these significant variables from GWPR model were mapped using GIS software. Those maps can depict the variations of influence of each factor on leptospirosis infection across the area of northeast region.

The study also indicated that using of the present algorithm to extract inundated areas from MODIS images is helpful in the temporal study. Geoinformatic technique is valuable in this study.

5.2 Recommendations

This study was the initiative in using geoinformatic technique to study the spatial epidemiology of leptospirosis in Thailand with the emphasized on northeast region. This region hold highest burden from leptospirosis as compare to other region of Thailand. Further study should be pointed out to this disease by using smaller aggregation unit of data in order to get more accurate results. Health personnel that responsible for leptospirosis surveillance and handle the data should aggregated raw data of the cases into district or even sub-district levels. If so, the analysis results will lead to more understanding of spatial process of leptospirosis transmission.

Other environmental data (that might affect the transmission of leptospirosis) such as, soil type, soil composition, salinity, and so on, were not available in this study. If these environmental variables were included in the analyses, the better explanation for leptospirosis transmission might be gained.

This work was a retrospective study that utilized a lot of secondary data and some types of data which were already occurred. Information biases can be easily arisen. These aspects should be considered in further study. On the other hand if the data are analyzed prospectively soon after the cases were recorded, the analysis results can be effectively used in the near-real-time disease warning system.

REFERENCES

REFERENCES

Anselin, L. (1999). Interactive techniques and exploratory spatial data analysis. In P. Longley, M. Goodchild, D. Maguire and D. Rhind (eds). **Geographical Information Systems: principles, techniques, management and applications.** (pp 251-264). New York: John Wiley:

Anselin, L. (2004). GeoDa 0.95i Release Notes. Spatial Analysis Laboratory (SAL). Department of Agricultural and Consumer Economics, University of Illinois, Urbana-Champaign, IL.

Anselin, L. (2005). Exploring Spatial Data with GeoDA: A Workbook. Spatial Analysis Laboratory (SAL), Department of Geography, University of Illinois, Urbana-Champaign, IL.

Arunagiri, A. (2009). World situation of leptospirosis. [Online]. Available: http://www.dgiri.com/node/20. [accessed 1 April 2009].

Bailey, T.C. (2001). Spatial statistical methods in health. **Cad Saude Publica.** 17: 1083-1098.

Barcellos, C. and Sabroza, P.C. (2001). The place behind the case: leptospirosis risks and associated environmental conditions in a flood-related outbreak in Rio de Janeiro. **Cad Saude Publica.** 17(Suppl): 59-67.

Bharti, A.R., Nally, J.E., Ricaldi, J.N., Matthias, M.A., Diaz, M.M., Lovett, M.A., Levett, P.N., Gilman, R.H., Willig, M.R., Gotuzzo, E. and Vinetz, J.M.

(2003). Leptospirosis: a zoonotic disease of global importance. **Lancet Infect Dis.** 3: 757-771.

Bunnag, T., Potha, U., Thirachandra, S. and Impand, P. (1983). Leptospirosis in man and rodents in North and Northeast Thailand. **Southeast Asian J Trop Med Public Health.** 14: 481-487.

Bureau of Epidemiology, Department of Disease Control, Ministry of Public Health, Thailand (2007). **Annual Epidemiological Surveillance Report.** [Online]. Available: http://epid.moph.go.th/Annual/ANNUAL2550/Annual_index.html [accessed 15 October 2009].

Bureau of Epidemiology, Department of Disease Control, Ministry of Public Health, Thailand. (2009). **Leptospirosis.** [Online]. Available: http://thaigcd.ddc.moph.go.th/zoo_knowledge_lepto.html [accessed 25 November 2009].

Bureau of Epidemiology, Department of Disease Control, Ministry of Public Health, Thailand. (2010). **Leptospirosis.** [Online]. Available: http://epid.moph.go.th/surdata/disease.php?ds=43 [accessed 12 March 2010].

Cline, B.L. (1970). New eyes for epidemiologists: Aerial photography and other remote sensing techniques. **Am J Epidemiol.** 92: 85-89.

Correia, V.R.M., Carvalho, M.S., Sabroza, P.C. and Vasconcelos, C.H. (2004). Remote sensing as a tool to survey endemic diseases in Brazil. **Cad Saude Publica.** 20(4): 891-904.

Douglin, C.P., Jordan, C., Rock, R., Hurley, A. and Levett, P.N. (1997). Risk factors for severe leptospirosis in the Parish of St. Andrew, Barbados. **Emerg Infect Dis.** 3: 78-80.

Faine, S., Adler, B., Bolin C. and Perolat, P. (1999). **Leptospira and leptospirosis.** Medisci, Melbourne.

Fotheringham, A.S., Brunsdon, C. and Chartlon, M. (2002). **Geographically Weighted Regression: The Analysis of Spatially Varying Relationships.** West Sussex, England: Wiley & Sons.

Gubler, D.J., Reiter, P., Ebi, K.L., Yap, W., Nasci, R. and Patz, L.A. (2001). Climate Variability and Change in the United States: Potential Impacts on Vector- and Rodent-Borne Diseases. **Environ Health Perspect.** 109 (Suppl 2): 223-233.

Jacquez, G.M. (n.d.). **Temporally Dynamic Aspatial and Geographically Weighted Regression in STIS: A Step by Step Guide.** [Online]. Available: http://www.terraseer.com/pdf/stis_regression_guide.pdf [accessed 11 January 2010].

Kaewpa, K. (2002). Factors Associated with Severe Leptospirosis in Khon Kaen Province, Thailand. M.S. Thesis, Collage of Public Health, University of the Philippines, Manila.

Kulldorff, M. (1997). A Spatial Scan Statistics. **Communication in Statistics-Theory and Methods.** 6(6): 1481-1496.

Kulldorff, M., Athas, W., Feurer, E., Miller, B. and Key, C. (1998). Evaluating cluster alarms: A space-time scan statistic and brain cancer in Los Alamos. **Am J Public Health.** 88: 1377-1380.

Kulldorff, M. and Information Management Services Inc. (2006). **SaTScan v7.0: Software for the spatial and space-time scan statistics.** [Computer software] Bethesda, MD, USA, National Cancer Institute. [Online]. Available: http://www.satscan.org/.

Kupek, E., de Sousa Santos Faversani, M.C. and de Souza Philippi, J.M. (2000). The relationship between rainfall and human leptospirosis in Florianópolis, Brazil, 1991-1996. **Braz J Infect Dis.** 4: 131-134.

Landis, J.R. and Koch, G.C. (1987). The measurement of observer agreement for categorical data. Biometric, 33: 159-179. ***(ชื่อ Joual อะไร?)***

Levett, P.N. (2001). Leptospirosis. **Clin Microbiol Rev.** 14: 296-326.

Maciel, E.A., de Carvalho, A.L., Nascimento, S.F., de Matos, R.B., Gouveia, E.L., Reis, M.G. and Ko, A.I. (2008). Household transmission of leptospira infection in urban slum communities. **PLoS Negl Trop Dis.** 2(1): e154.

Michel, V., Branger, C. and Andre-Fontaine, G. (2002). Epidemiology of leptospirosis. **Rev Cubana Med Trop.** 54: 7-10.

Ministry of Public Health of Thailand. (1999). Leptospirosis manual: Thai edition, ISBN 974-7897-90-3. Bangkok, Thailand.

Nakaya, T., Fotheringham, A.S., Brunsdon, C. and Chartlon, M. (2005). Geographically weighted regression for disease association mapping. **Statist Med.** 24: 2695-2717.

Nobre, F.F. and Carvalho, M.S. (1996). Spatial and Temporal Analysis of Epidemiological Data. In: D. Savigny and P. Wijeyaratene. (Org.). GIS for Health and the Environment. Ottawa, Canada: IDRC Focus Series, 1996.

Odoi, A., Martin, S.W., Michel, P., Holt, J,, Middleton, D. and Wilson, J. (2004). Geographical and temporal distribution of human giardiasis in Ontario, Canada. **Int J Health Geographics.** [Online]. Available: http://www.ij-healthgeographics.com/content/3/1/11 [accessed 25 March 2006].

Ostfeld, R.S., Glass, G.E. and Keesing, F. (2005). Spatial epidemiology: an emerging (or re-emerging) discipline. **TRENDS in Ecology and Evolution.** 20: 328-336.

Pappas. G., Papadimitriou. P., Siozopoulou. V., Christou. L. and Akritidis. N. (2008). The globalization of leptospirosis: worldwide incidence trends. **Int J Infect Dis.** 12(4): 351-357.

Pfeiffer, D., Robinson, T., Stevenson, M., Stevens, K., Rogers, D. and Clements, A. (2008). **Spatial Analysis in Epidemiology.** New York: Oxford University Press.

Riccardo, F. and Bayugo, Y.V. (n.d.). **Leptospirosis in South East Asia: the tip of the iceberg?** [Online]. Available: http://www.searo.who.int/LinkFiles/Communicable_Diseases_Surveillance_and_response_Leptospirosis_in_South_East_Asia.pdf. [accessed 11 March 2009].

Rothman, K.J. (1990). A sobering start for the cluster busters, conference. **Am J Epidemiol.** 132 (Suppl): S6-S13.

Rushton G. (2003). Public Health, GIS, and Spatial Analytic Tools. **Annu Rev Public Health.** 24: 43-56.

Sasaki, D.M., Pang, L., Minette, H.P., Wakida, C.K., Fujimoto, W.J., Manea, S.J., Kunioka, R. and Middleton, C.R. (1993). Active Surveillance and Risk Factors for Leptospirosis in Hawaii. **Am J Trop Med Hyg.** 48: 35-43.

Sehgal S.C. (2006). Epidemiological patterns of leptospirosis. **Indian J Med Microbiol.** 24: 310-311.

Sugunan, A.P., Vijayachari, P., Sharma, S., Roy, S., Manickam, P., Natarajaseenivasan, K., Gupte, M.D. and Sehgal, S.C. (2009). Risk factors associated with leptospirosis during an outbreak in Middle Andaman, India. **Indian J Med Res.** 130: 67-73.

Sundharagiati B., Harinasuta, C. and Photha, U. (1966). Human leptospirosis in Thailand. **Tran R Soc Trop Med Hyg.** 60: 361-365.

Takeuchi, W., Nemoto, T., Baruah, P.J, Cchi, S. and Yasuoka, Y. (2003). Development of Terra MODIS data pre-processing system on WWW. **J Japan Photogram Remote Sensing.** 42: 21-27. [Online]. Available: http://webmodis.iis.u-tokyo.ac.jp/ [accessed 12 March 2006].

Takeuchi, W. and Yasuoka, Y. (2004). Development of normalized vegetation, soil and water indices (NDXI) with satellite remote sensing data, **J Japan Photogram Remote Sensing.** 43: 7-19.

Tangkanakul, W., Naigowit, P., Smithsuwan, P., Kaewmalang, P,, Khoprasert, Y. and Phulsuksombati, D. (2000). Prevalence of asymptomatic leptospirosis infection among high risk group 1998. **J Health Science.** 9: 56-62.

Tangkanakul, W., Smits, H.L., Jatanasen, S. and Ashford, D.A. (2005). Leptospirosis: an emerging health problem in Thailand. **Southeast Asian J Trop Med Public Health.** 36: 281-288.

Tangkanakul, W., Tharmaphornpil, P., Plikaytis, B.D., Bragg, S., Phulsuksombati, D., Choomkasien, P., Kingnate, D. and Ashford D.A. (2000). Risk factors associated with leptospirosis in Northeastern Thailand, 1998. **Am J Trop Med Hyg.** 63: 204-208.

Tassinari, W.S., Pellegrini, D.C., Sá, C,B,, Reis, R.B., Ko, A.I. and Carvalho, M.S. (2008). Detection and modelling of case clusters for urban leptospirosis. **Trop Med Int Health.** 13: 503-512.

The Leptospirosis Information Center. (n.d.). Life cycle of pathogenic leptospires. [Online]. Available: © 2004-2009 www.leptospirosis.org [Accessed 24 April 2010].

The National Statistical Office, Kingdom Of Thailand. (2008). Survey of population migration: The summary for administrator. [Online]. Available: http://service.nso.go.th/nso/nsopublish/service/survey/MigrantExec51.pdf [Accessed 22 March 2010].

Tu, J. and Xia, Z.-G. (2008). Examining spatially varying relationships between land use and water quality using geographically weighted regression I: Model design and evaluation. **Science Total Environ.** 407(1): 358-378.

Wangroongsarb, P., Petkanchanapong, W., Yasaeng, S., Imvithaya, A. and Naigowit, P. (2002). Survey of leptospirosis among rodents in endemic areas of Thailand. **J Trop Med Parasitol.** 25: 55-58.

Watt, G. Leptospirosis. (1997). **Curr Opin Infect Dis.** 10: 149-152.

Xiao, X., Boles, S., Liu, J., Zhuang, D., Frolking, S., Li, C., Salas, W. and Moore, B. (2005). Mapping paddy rice agriculture in southern China using multi-temporal MODIS images. **Remote Sensing of Environment.** 95: 480-492.

Xiao, X., Boles, S., Frolking, S., Li, C., Babu, J.Y., Salas, W. and Moore, B. (2006). Mapping paddy rice agriculture in South and Southeast Asia using multi-temporal MODIS images. **Remote Sensing of Environment.** 100: 95-113.

REFERENCES

REFERENCES

Anselin, L. (1999). Interactive techniques and exploratory spatial data analysis. In P. Longley, M. Goodchild, D. Maguire and D. Rhind (eds). **Geographical Information Systems: principles, techniques, management and applications.** (pp 251-264). New York: John Wiley:

Anselin, L. (2004). GeoDa 0.95i Release Notes. Spatial Analysis Laboratory (SAL). Department of Agricultural and Consumer Economics, University of Illinois, Urbana-Champaign, IL.

Anselin, L. (2005). Exploring Spatial Data with GeoDA: A Workbook. Spatial Analysis Laboratory (SAL), Department of Geography, University of Illinois, Urbana-Champaign, IL.

Arunagiri, A. (2009). World situation of leptospirosis. [Online]. Available: http://www.dgiri.com/node/20. [accessed 1 April 2009].

Bailey, T.C. (2001). Spatial statistical methods in health. **Cad Saude Publica.** 17: 1083-1098.

Barcellos, C. and Sabroza, P.C. (2001). The place behind the case: leptospirosis risks and associated environmental conditions in a flood-related outbreak in Rio de Janeiro. **Cad Saude Publica.** 17(Suppl): 59-67.

Bharti, A.R., Nally, J.E., Ricaldi, J.N., Matthias, M.A., Diaz, M.M., Lovett, M.A., Levett, P.N., Gilman, R.H., Willig, M.R., Gotuzzo, E. and Vinetz, J.M.

(2003). Leptospirosis: a zoonotic disease of global importance. **Lancet Infect Dis.** 3: 757-771.

Bunnag, T., Potha, U., Thirachandra, S. and Impand, P. (1983). Leptospirosis in man and rodents in North and Northeast Thailand. **Southeast Asian J Trop Med Public Health.** 14: 481-487.

Bureau of Epidemiology, Department of Disease Control, Ministry of Public Health, Thailand (2007). **Annual Epidemiological Surveillance Report.** [Online]. Available: http://epid.moph.go.th/Annual/ANNUAL2550/Annual_index.html [accessed 15 October 2009].

Bureau of Epidemiology, Department of Disease Control, Ministry of Public Health, Thailand. (2009). **Leptospirosis.** [Online]. Available: http://thaigcd.ddc.moph.go.th/zoo_knowledge_lepto.html [accessed 25 November 2009].

Bureau of Epidemiology, Department of Disease Control, Ministry of Public Health, Thailand. (2010). **Leptospirosis.** [Online]. Available: http://epid.moph.go.th/surdata/disease.php?ds=43 [accessed 12 March 2010].

Cline, B.L. (1970). New eyes for epidemiologists: Aerial photography and other remote sensing techniques. **Am J Epidemiol.** 92: 85-89.

Correia, V.R.M., Carvalho, M.S., Sabroza, P.C. and Vasconcelos, C.H. (2004). Remote sensing as a tool to survey endemic diseases in Brazil. **Cad Saude Publica.** 20(4): 891-904.

Douglin, C.P., Jordan, C., Rock, R., Hurley, A. and Levett, P.N. (1997). Risk factors for severe leptospirosis in the Parish of St. Andrew, Barbados. **Emerg Infect Dis.** 3: 78-80.

Faine, S., Adler, B., Bolin C. and Perolat, P. (1999). **Leptospira and leptospirosis.** Medisci, Melbourne.

Fotheringham, A.S., Brunsdon, C. and Chartlon, M. (2002). **Geographically Weighted Regression: The Analysis of Spatially Varying Relationships.** West Sussex, England: Wiley & Sons.

Gubler, D.J., Reiter, P., Ebi, K.L., Yap, W., Nasci, R. and Patz, L.A. (2001). Climate Variability and Change in the United States: Potential Impacts on Vector- and Rodent-Borne Diseases. **Environ Health Perspect.** 109 (Suppl 2): 223-233.

Jacquez, G.M. (n.d.). **Temporally Dynamic Aspatial and Geographically Weighted Regression in STIS: A Step by Step Guide.** [Online]. Available: http://www.terraseer.com/pdf/stis_regression_guide.pdf [accessed 11 January 2010].

Kaewpa, K. (2002). Factors Associated with Severe Leptospirosis in Khon Kaen Province, Thailand. M.S. Thesis, Collage of Public Health, University of the Philippines, Manila.

Kulldorff, M. (1997). A Spatial Scan Statistics. **Communication in Statistics-Theory and Methods.** 6(6): 1481-1496.

Kulldorff, M., Athas, W., Feurer, E., Miller, B. and Key, C. (1998). Evaluating cluster alarms: A space-time scan statistic and brain cancer in Los Alamos. **Am J Public Health.** 88: 1377-1380.

Kulldorff, M. and Information Management Services Inc. (2006). **SaTScan v7.0: Software for the spatial and space-time scan statistics.** [Computer software] Bethesda, MD, USA, National Cancer Institute. [Online]. Available: http://www.satscan.org/.

Kupek, E., de Sousa Santos Faversani, M.C. and de Souza Philippi, J.M. (2000). The relationship between rainfall and human leptospirosis in Florianópolis, Brazil, 1991-1996. **Braz J Infect Dis.** 4: 131-134.

Landis, J.R. and Koch, G.C. (1987). The measurement of observer agreement for categorical data. Biometric, 33: 159-179. ***(ชื่อ Joual อะไร?)***

Levett, P.N. (2001). Leptospirosis. **Clin Microbiol Rev.** 14: 296-326.

Maciel, E.A., de Carvalho, A.L., Nascimento, S.F., de Matos, R.B., Gouveia, E.L., Reis, M.G. and Ko, A.I. (2008). Household transmission of leptospira infection in urban slum communities. **PLoS Negl Trop Dis.** 2(1): e154.

Michel, V., Branger, C. and Andre-Fontaine, G. (2002). Epidemiology of leptospirosis. **Rev Cubana Med Trop.** 54: 7-10.

Ministry of Public Health of Thailand. (1999). Leptospirosis manual: Thai edition, ISBN 974-7897-90-3. Bangkok, Thailand.

Nakaya, T., Fotheringham, A.S., Brunsdon, C. and Chartlon, M. (2005). Geographically weighted regression for disease association mapping. **Statist Med.** 24: 2695-2717.

Nobre, F.F. and Carvalho, M.S. (1996). Spatial and Temporal Analysis of Epidemiological Data. In: D. Savigny and P. Wijeyaratene. (Org.). GIS for Health and the Environment. Ottawa, Canada: IDRC Focus Series, 1996.

Odoi, A., Martin, S.W., Michel, P., Holt, J,, Middleton, D. and Wilson, J. (2004). Geographical and temporal distribution of human giardiasis in Ontario, Canada. **Int J Health Geographics.** [Online]. Available: http://www.ij-healthgeographics.com/content/3/1/11 [accessed 25 March 2006].

Ostfeld, R.S., Glass, G.E. and Keesing, F. (2005). Spatial epidemiology: an emerging (or re-emerging) discipline. **TRENDS in Ecology and Evolution.** 20: 328-336.

Pappas. G., Papadimitriou. P., Siozopoulou. V., Christou. L. and Akritidis. N. (2008). The globalization of leptospirosis: worldwide incidence trends. **Int J Infect Dis.** 12(4): 351-357.

Pfeiffer, D., Robinson, T., Stevenson, M., Stevens, K., Rogers, D. and Clements, A. (2008). **Spatial Analysis in Epidemiology.** New York: Oxford University Press.

Riccardo, F. and Bayugo, Y.V. (n.d.). **Leptospirosis in South East Asia: the tip of the iceberg?** [Online]. Available: http://www.searo.who.int/LinkFiles/Communicable_Diseases_Surveillance_and_response_Leptospirosis_in_South_East_Asia.pdf. [accessed 11 March 2009].

Rothman, K.J. (1990). A sobering start for the cluster busters, conference. **Am J Epidemiol.** 132 (Suppl): S6-S13.

Rushton G. (2003). Public Health, GIS, and Spatial Analytic Tools. **Annu Rev Public Health.** 24: 43-56.

Sasaki, D.M., Pang, L., Minette, H.P., Wakida, C.K., Fujimoto, W.J., Manea, S.J., Kunioka, R. and Middleton, C.R. (1993). Active Surveillance and Risk Factors for Leptospirosis in Hawaii. **Am J Trop Med Hyg.** 48: 35-43.

Sehgal S.C. (2006). Epidemiological patterns of leptospirosis. **Indian J Med Microbiol.** 24: 310-311.

Sugunan, A.P., Vijayachari, P., Sharma, S., Roy, S., Manickam, P., Natarajaseenivasan, K., Gupte, M.D. and Sehgal, S.C. (2009). Risk factors associated with leptospirosis during an outbreak in Middle Andaman, India. **Indian J Med Res.** 130: 67-73.

Sundharagiati B., Harinasuta, C. and Photha, U. (1966). Human leptospirosis in Thailand. **Tran R Soc Trop Med Hyg.** 60: 361-365.

Takeuchi, W., Nemoto, T., Baruah, P.J, Cchi, S. and Yasuoka, Y. (2003). Development of Terra MODIS data pre-processing system on WWW. **J Japan Photogram Remote Sensing.** 42: 21-27. [Online]. Available: http://webmodis.iis.u-tokyo.ac.jp/ [accessed 12 March 2006].

Takeuchi, W. and Yasuoka, Y. (2004). Development of normalized vegetation, soil and water indices (NDXI) with satellite remote sensing data, **J Japan Photogram Remote Sensing.** 43: 7-19.

Tangkanakul, W., Naigowit, P., Smithsuwan, P., Kaewmalang, P,, Khoprasert, Y. and Phulsuksombati, D. (2000). Prevalence of asymptomatic leptospirosis infection among high risk group 1998. **J Health Science.** 9: 56-62.

Tangkanakul, W., Smits, H.L., Jatanasen, S. and Ashford, D.A. (2005). Leptospirosis: an emerging health problem in Thailand. **Southeast Asian J Trop Med Public Health.** 36: 281-288.

Tangkanakul, W., Tharmaphornpil, P., Plikaytis, B.D., Bragg, S., Phulsuksombati, D., Choomkasien, P., Kingnate, D. and Ashford D.A. (2000). Risk factors associated with leptospirosis in Northeastern Thailand, 1998. **Am J Trop Med Hyg.** 63: 204-208.

Tassinari, W.S., Pellegrini, D.C., Sá, C,B,, Reis, R.B., Ko, A.I. and Carvalho, M.S. (2008). Detection and modelling of case clusters for urban leptospirosis. **Trop Med Int Health.** 13: 503-512.

The Leptospirosis Information Center. (n.d.). Life cycle of pathogenic leptospires. [Online]. Available: © 2004-2009 www.leptospirosis.org [Accessed 24 April 2010].

The National Statistical Office, Kingdom Of Thailand. (2008). Survey of population migration: The summary for administrator. [Online]. Available: http://service.nso.go.th/nso/nsopublish/service/survey/MigrantExec51.pdf [Accessed 22 March 2010].

Tu, J. and Xia, Z.-G. (2008). Examining spatially varying relationships between land use and water quality using geographically weighted regression I: Model design and evaluation. **Science Total Environ.** 407(1): 358-378.

Wangroongsarb, P., Petkanchanapong, W., Yasaeng, S., Imvithaya, A. and Naigowit, P. (2002). Survey of leptospirosis among rodents in endemic areas of Thailand. **J Trop Med Parasitol.** 25: 55-58.

Watt, G. Leptospirosis. (1997). **Curr Opin Infect Dis.** 10: 149-152.

Xiao, X., Boles, S., Liu, J., Zhuang, D., Frolking, S., Li, C., Salas, W. and Moore, B. (2005). Mapping paddy rice agriculture in southern China using multi-temporal MODIS images. **Remote Sensing of Environment.** 95: 480-492.

Xiao, X., Boles, S., Frolking, S., Li, C., Babu, J.Y., Salas, W. and Moore, B. (2006). Mapping paddy rice agriculture in South and Southeast Asia using multi-temporal MODIS images. **Remote Sensing of Environment.** 100: 95-113.

APPENDICES

APPENDIX A

LEPTOSPIROSIS INCIDENCE RATE BY PROVINCE

The raw incidence rates, SEB smoothed incidence rates and excess risk by province was summarized annually in separated tables. Raw incidence rates and smoothed incidence rates of each year were put together in order to facilitate the comparison of these rates in each province. Table A1 to A7 expressed the rates of 2003 to 2009, respectively.

Table A1 Raw and SEB smoothed incidence rates and excess risks by province, 2003.

Region	Province	Raw Incidence Rate (per 100,000)	SEB Smoothed Incidence Rate (per 100,000)	Excess Risk
	Bangkok	0.02	0.02	0.00
	Samut Prakarn	0.00	0.02	0.00
	Nonthaburi	0.00	0.03	0.00
	Pathum Thani	0.55	0.55	0.07
	Phra Nakhon Sri Ayuthay	1.20	1.20	0.15
	Ang Thong	2.41	1.48	0.31
	Lop Buri	0.65	0.89	0.08
	Sing Buri	0.90	1.08	0.11
	Chai Nat	8.00	7.27	1.02
	Saraburi	4.17	4.19	0.53
C	Chon Buri	0.09	0.15	0.01
E	Rayong	4.17	3.92	0.53
N	Chanthaburi	2.36	2.27	0.30
T	Trat	0.00	0.81	0.00
R	Chachoengsao	0.46	0.46	0.06
A	Prachin Buri	0.88	1.34	0.11
L	Nakhom Nayok	1.99	2.39	0.25
	Sa Kaeo	3.33	3.49	0.42
	Ratchaburi	0.12	0.30	0.02
	Kanchanaburi	0.75	0.76	0.10
	Suphanburi	1.73	1.74	0.22
	Nakhon Pathom	0.25	0.26	0.03
	Samut Sakhon	0.00	0.04	0.00
	Samut Songkhram	0.49	0.28	0.06
	Phetchaburi	0.65	0.45	0.08
	Prachuap Khiri Khan	0.82	1.02	0.10
	Chiang Mai	1.63	1.67	0.21
	Lamphun	0.25	0.36	0.03
	Lamphang	20.53	20.34	2.60
	Uttaradit	4.14	4.26	0.53
	Phrae	20.26	19.99	2.57
	Nan	16.29	16.20	2.07
N	Phayao	19.40	18.87	2.46
O	Chiang Rai	11.01	11.00	1.40
R	Mae Hong Son	2.51	1.84	0.32
T	Nakhon Sawan	1.06	1.11	0.14
H	Uthai Thani	3.55	3.35	0.45
	Kamphaeng Phet	1.43	1.44	0.18
	Tak	0.00	0.06	0.00
	Sukhothai	0.32	0.44	0.04
	Phitsanulok	4.61	4.63	0.59
	Phichit	1.01	1.22	0.13
	Phetchabun	5.83	5.88	0.74

Table A1 (Continued).

Region	Province	Raw Incidence Rate (per 100,000)	SEB Smoothed Incidence Rate (per 100,000)	Excess Risk
	Nakhom Ratchasima	8.12	8.15	1.03
	Burirum	23.55	23.48	2.99
	Surin	24.73	24.83	3.14
	Sisaket	40.42	40.21	5.13
	Ubon Ratchathani	14.23	14.28	1.81
N	Yasothon	5.42	5.80	0.69
O	Chaiyaphum	10.99	11.01	1.39
R	Amnat Charoen	7.56	7.93	0.96
T	Nong Bua Lam Phu	13.42	13.62	1.70
H	Khon Kaen	31.09	30.92	3.94
E	Udon Thani	6.63	6.75	0.84
A	Loei	22.39	22.22	2.84
S	Nong Khai	11.85	11.77	1.50
T	Maha Sarakhom	14.62	15.69	1.86
	Roi Et	32.28	32.18	4.10
	Kalasin	25.90	25.80	3.29
	Sakon Nakhon	6.93	6.97	0.88
	Nakhon Phanom	0.28	0.56	0.04
	Mukdahan	2.36	2.72	0.30
	Nakhon Sri Thammarat	2.87	2.69	0.36
	Krabi	2.36	2.45	0.30
	Phangnga	11.25	10.11	1.43
	Phuket	1.46	7.95	0.19
S	Surat Thani	2.59	2.65	0.33
O	Ranong	7.35	6.63	0.93
U	Chumphon	2.31	2.35	0.29
T	Songkhla	0.86	0.96	0.11
H	Satun	1.10	1.05	0.14
	Trang	0.99	1.59	0.13
	Phatthalung	1.59	1.63	0.20
	Pattani	0.16	0.53	0.02
	Yala	1.95	1.49	0.25
	Narathiwat	1.56	1.44	0.20

Table A2 Raw and SEB smoothed incidence rates and excess risks by province, 2004.

Region	Province	Raw Incidence Rate (per 100,000)	SEB Smoothed Incidence Rate (per 100,000)	Excess Risk
CENTRAL	Bangkok	0.09	0.10	0.02
	Samut Prakarn	0.00	0.06	0.00
	Nonthaburi	0.32	0.22	0.06
	Pathum Thani	0.40	0.40	0.08
	Phra Nakhon Sri Ayuthay	0.40	0.47	0.08
	Ang Thong	1.74	0.91	0.34
	Lop Buri	0.79	1.01	0.16
	Sing Buri	0.90	1.03	0.18
	Chai Nat	5.21	4.48	1.02
	Saraburi	2.95	2.99	0.58
	Chon Buri	0.17	0.22	0.03
	Rayong	2.36	2.35	0.46
	Chanthaburi	6.76	6.41	1.32
	Trat	0.00	0.95	0.00
	Chachoengsao	0.46	0.47	0.09
	Prachin Buri	1.56	2.04	0.30
	Nakhom Nayok	2.40	2.66	0.47
	Sa Kaeo	3.71	3.93	0.73
	Ratchaburi	0.85	0.74	0.17
	Kanchanaburi	1.00	0.92	0.20
	Suphanburi	1.17	1.17	0.23
	Nakhon Pathom	0.00	0.08	0.00
	Samut Sakhon	0.00	0.06	0.00
	Samut Songkhram	0.00	0.23	0.00
	Phetchaburi	0.00	0.32	0.00
	Prachuap Khiri Khan	0.41	0.51	0.08
NORTH	Chiang Mai	2.10	2.16	0.41
	Lamphun	0.74	0.99	0.14
	Lamphang	6.47	6.37	1.27
	Uttaradit	5.67	5.65	1.11
	Phrae	10.26	9.94	2.00
	Nan	10.21	9.93	2.00
	Phayao	11.72	11.03	2.29
	Chiang Rai	4.12	4.14	0.81
	Mae Hong Son	4.56	3.39	0.89
	Nakhon Sawan	0.64	0.67	0.12
	Uthai Thani	1.80	1.69	0.35
	Kamphaeng Phet	0.00	0.08	0.00
	Tak	0.39	0.52	0.08
	Sukhothai	0.49	0.65	0.10
	Phitsanulok	3.39	3.41	0.66
	Phichit	0.00	0.18	0.00
	Phetchabun	3.60	3.64	0.70

Table A2 (Continued).

Region	Province	Raw Incidence Rate (per 100,000)	SEB Smoothed Incidence Rate (per 100,000)	Excess Risk
	Nakhom Ratchasima	6.24	6.25	1.22
	Burirum	13.90	13.88	2.72
	Surin	26.93	26.66	5.26
	Sisaket	10.19	10.23	1.99
	Ubon Ratchathani	6.50	6.67	1.27
N	Yasothon	14.44	13.08	2.82
O	Chaiyaphum	4.70	4.78	0.92
R	Amnat Charoen	7.32	7.55	1.43
T	Nong Bua Lam Phu	11.26	11.29	2.20
H	Khon Kaen	11.96	11.95	2.34
E	Udon Thani	5.16	5.22	1.01
A	Loei	28.67	28.06	5.61
S	Nong Khai	8.84	8.83	1.73
T	Maha Sarakhom	6.07	6.27	1.19
	Roi Et	10.48	10.56	2.05
	Kalasin	38.25	37.96	7.48
	Sakon Nakhon	3.61	3.66	0.71
	Nakhon Phanom	0.71	0.99	0.14
	Mukdahan	9.53	9.61	1.86
	Nakhon Sri Thammarat	2.11	2.11	0.41
	Krabi	0.26	0.55	0.05
	Phangnga	6.25	5.53	1.22
	Phuket	1.77	7.95	0.35
S	Surat Thani	1.17	1.29	0.23
O	Ranong	5.30	4.48	1.04
U	Chumphon	4.00	3.70	0.78
T	Songkhla	1.09	1.14	0.21
H	Satun	0.00	0.30	0.00
	Trang	7.64	7.28	1.49
	Phatthalung	1.79	1.85	0.35
	Pattani	0.00	0.36	0.00
	Yala	2.16	1.86	0.42
	Narathiwat	2.28	2.13	0.45

Table A3 Raw and SEB smoothed incidence rates and excess risks by province, 2005.

Region	Province	Raw Incidence Rate (per 100,000)	SEB Smoothed Incidence Rate (per 100,000)	Excess Risk
	Bangkok	0.05	0.06	0.01
	Samut Prakarn	0.09	0.10	0.02
	Nonthaburi	0.63	0.49	0.14
	Pathum Thani	0.13	0.15	0.03
	Phra Nakhon Sri Ayuthay	0.67	0.72	0.15
	Ang Thong	1.06	1.06	0.23
	Lop Buri	1.47	1.65	0.32
	Sing Buri	1.37	1.33	0.30
	Chai Nat	3.52	3.16	0.76
	Saraburi	3.17	3.10	0.69
C	Chon Buri	0.26	0.31	0.06
E	Rayong	1.27	1.28	0.28
N	Chanthaburi	3.83	3.55	0.83
T	Trat	0.00	0.90	0.00
R	Chachoengsao	0.46	0.47	0.10
A	Prachin Buri	0.67	1.28	0.15
L	Nakhom Nayok	2.00	2.18	0.43
	Sa Kaeo	3.91	3.90	0.85
	Ratchaburi	0.37	0.23	0.08
	Kanchanaburi	0.37	0.41	0.08
	Suphanburi	0.95	0.97	0.21
	Nakhon Pathom	0.25	0.26	0.05
	Samut Sakhon	0.00	0.08	0.00
	Samut Songkhram	0.00	0.16	0.00
	Phetchaburi	0.00	0.28	0.00
	Prachuap Khiri Khan	0.83	0.92	0.18
	Chiang Mai	3.23	3.26	0.70
	Lamphun	0.99	1.38	0.21
	Lamphang	7.97	7.93	1.73
	Uttaradit	4.68	4.71	1.02
	Phrae	7.62	7.70	1.65
	Nan	17.79	17.63	3.86
N	Phayao	25.84	25.31	5.60
O	Chiang Rai	3.36	3.40	0.73
R	Mae Hong Son	13.67	12.46	2.97
T	Nakhon Sawan	0.84	0.90	0.18
H	Uthai Thani	5.21	4.45	1.13
	Kamphaeng Phet	0.00	0.27	0.00
	Tak	1.35	1.42	0.29
	Sukhothai	0.49	0.63	0.11
	Phitsanulok	1.43	1.46	0.31
	Phichit	0.18	0.37	0.04
	Phetchabun	2.79	2.85	0.61

Table A3 (Continued).

Region	Province	Raw Incidence Rate (per 100,000)	SEB Smoothed Incidence Rate (per 100,000)	Excess Risk
	Nakhom Ratchasima	4.36	4.39	0.95
	Burirum	5.43	5.49	1.18
	Surin	9.54	9.54	2.07
	Sisaket	16.64	16.38	3.61
	Ubon Ratchathani	4.81	4.90	1.04
N	Yasothon	11.82	11.66	2.56
O	Chaiyaphum	6.62	6.62	1.44
R	Amnat Charoen	3.80	4.20	0.83
T	Nong Bua Lam Phu	5.65	6.48	1.23
H	Khon Kaen	13.87	13.75	3.01
E	Udon Thani	8.87	9.01	1.93
A	Loei	19.46	19.10	4.22
S	Nong Khai	20.09	19.85	4.36
T	Maha Sarakhom	3.85	4.25	0.83
	Roi Et	10.30	10.34	2.23
	Kalasin	15.53	15.14	3.37
	Sakon Nakhon	6.53	6.62	1.42
	Nakhon Phanom	0.72	0.91	0.16
	Mukdahan	4.50	4.94	0.98
	Nakhon Sri Thammarat	2.00	2.04	0.43
	Krabi	0.51	0.70	0.11
	Phangnga	11.65	10.99	2.53
	Phuket	4.15	7.95	0.90
S	Surat Thani	0.85	0.92	0.18
O	Ranong	4.51	4.37	0.98
U	Chumphon	4.43	4.07	0.96
T	Songkhla	4.26	4.08	0.92
H	Satun	0.00	1.14	0.00
	Trang	5.51	5.09	1.20
	Phatthalung	1.40	1.73	0.30
	Pattani	0.16	0.58	0.03
	Yala	2.60	2.77	0.56
	Narathiwat	6.60	6.40	1.43

Table A4 Raw and SEB smoothed incidence rates and excess risks by province, 2006.

Region	Province	Raw Incidence Rate (per 100,000)	SEB Smoothed Incidence Rate (per 100,000)	Excess Risk
CENTRAL	Bangkok	0.14	0.16	0.02
	Samut Prakarn	0.55	0.43	0.09
	Nonthaburi	0.41	0.41	0.06
	Pathum Thani	0.12	0.14	0.02
	Phra Nakhon Sri Ayuthay	3.06	3.01	0.49
	Ang Thong	1.76	2.01	0.28
	Lop Buri	2.13	2.47	0.34
	Sing Buri	7.82	6.89	1.24
	Chai Nat	9.13	8.40	1.45
	Saraburi	8.09	7.55	1.29
	Chon Buri	0.59	0.62	0.09
	Rayong	6.53	6.54	1.04
	Chanthaburi	23.39	23.04	3.72
	Trat	1.37	2.47	0.22
	Chachoengsao	0.77	0.78	0.12
	Prachin Buri	0.66	1.09	0.11
	Nakhom Nayok	0.80	1.20	0.13
	Sa Kaeo	8.00	7.94	1.27
	Ratchaburi	0.36	0.34	0.06
	Kanchanaburi	0.24	0.30	0.04
	Suphanburi	1.54	1.58	0.25
	Nakhon Pathom	0.00	0.05	0.00
	Samut Sakhon	0.22	0.20	0.04
	Samut Songkhram	1.54	0.62	0.24
	Phetchaburi	0.44	0.63	0.07
	Prachuap Khiri Khan	1.02	1.14	0.16
NORTH	Chiang Mai	4.53	4.64	0.72
	Lamphun	0.99	1.66	0.16
	Lamphang	10.96	10.85	1.74
	Uttaradit	4.06	4.12	0.65
	Phrae	12.98	13.02	2.06
	Nan	67.17	66.79	10.67
	Phayao	21.17	21.15	3.36
	Chiang Rai	7.43	7.46	1.18
	Mae Hong Son	10.22	7.99	1.62
	Nakhon Sawan	1.95	2.02	0.31
	Uthai Thani	4.90	4.67	0.78
	Kamphaeng Phet	0.00	0.15	0.00
	Tak	6.29	6.14	1.00
	Sukhothai	0.33	0.51	0.05
	Phitsanulok	2.73	2.76	0.43
	Phichit	0.90	1.09	0.14
	Phetchabun	5.09	5.14	0.81

Table A4 (Continued).

Region	Province	Raw Incidence Rate (per 100,000)	SEB Smoothed Incidence Rate (per 100,000)	Excess Risk
	Nakhom Ratchasima	4.15	4.19	0.66
	Burirum	7.82	7.85	1.24
	Surin	12.07	12.06	1.92
	Sisaket	22.70	22.47	3.61
	Ubon Ratchathani	6.97	7.05	1.11
N	Yasothon	10.90	10.90	1.73
O	Chaiyaphum	6.17	6.21	0.98
R	Amnat Charoen	5.42	5.85	0.86
T	Nong Bua Lam Phu	1.41	1.89	0.22
H	Khon Kaen	19.90	19.79	3.16
E	Udon Thani	5.51	5.65	0.88
A	Loei	18.44	18.23	2.93
S	Nong Khai	20.27	20.04	3.22
T	Maha Sarakhom	4.48	4.71	0.71
	Roi Et	6.03	6.15	0.96
	Kalasin	24.01	23.76	3.82
	Sakon Nakhon	7.95	7.99	1.26
	Nakhon Phanom	0.14	0.34	0.02
	Mukdahan	2.09	2.42	0.33
	Nakhon Sri Thammarat	3.12	3.15	0.50
	Krabi	2.25	2.38	0.36
	Phangnga	15.61	15.33	2.48
	Phuket	5.06	7.95	0.80
S	Surat Thani	0.84	0.89	0.13
O	Ranong	29.05	28.00	4.62
U	Chumphon	5.45	5.43	0.87
T	Songkhla	5.50	5.23	0.87
H	Satun	0.36	1.12	0.06
	Trang	11.08	10.68	1.76
	Phatthalung	1.79	2.07	0.29
	Pattani	2.36	3.07	0.38
	Yala	3.43	3.92	0.55
	Narathiwat	6.68	6.28	1.06

Table A5 Raw and SEB smoothed incidence rates and excess risks by province, 2007.

Region	Province	Raw Incidence Rate (per 100,000)	SEB Smoothed Incidence Rate (per 100,000)	Excess Risk
CENTRAL	Bangkok	0.04	0.05	0.01
	Samut Prakarn	0.54	0.42	0.11
	Nonthaburi	0.10	0.11	0.02
	Pathum Thani	0.23	0.25	0.05
	Phra Nakhon Sri Ayuthay	2.39	2.08	0.46
	Ang Thong	1.06	1.33	0.21
	Lop Buri	1.20	1.59	0.23
	Sing Buri	0.46	0.75	0.09
	Chai Nat	7.96	7.22	1.54
	Saraburi	1.15	1.39	0.22
	Chon Buri	0.25	0.28	0.05
	Rayong	2.44	2.46	0.47
	Chanthaburi	9.95	9.64	1.93
	Trat	0.91	2.02	0.18
	Chachoengsao	0.31	0.32	0.06
	Prachin Buri	0.44	0.73	0.09
	Nakhom Nayok	2.00	1.80	0.39
	Sa Kaeo	7.06	6.99	1.37
	Ratchaburi	1.33	1.13	0.26
	Kanchanaburi	0.72	0.84	0.14
	Suphanburi	1.07	1.09	0.21
	Nakhon Pathom	0.12	0.16	0.02
	Samut Sakhon	0.00	0.04	0.00
	Samut Songkhram	0.00	0.27	0.00
	Phetchaburi	0.00	0.32	0.00
	Prachuap Khiri Khan	0.61	0.64	0.12
NORTH	Chiang Mai	2.41	2.47	0.47
	Lamphun	1.23	1.74	0.24
	Lamphang	5.04	5.06	0.98
	Uttaradit	3.64	3.69	0.71
	Phrae	5.55	5.64	1.08
	Nan	16.96	16.62	3.29
	Phayao	17.48	16.85	3.39
	Chiang Rai	11.01	10.93	2.14
	Mae Hong Son	3.92	2.49	0.76
	Nakhon Sawan	1.77	1.79	0.34
	Uthai Thani	1.53	1.58	0.30
	Kamphaeng Phet	0.55	1.16	0.11
	Tak	1.71	1.76	0.33
	Sukhothai	0.99	1.22	0.19
	Phitsanulok	2.25	2.29	0.44
	Phichit	1.43	1.62	0.28
	Phetchabun	3.79	3.83	0.74

Table A5 (Continued).

Region	Province	Raw Incidence Rate (per 100,000)	SEB Smoothed Incidence Rate (per 100,000)	Excess Risk
	Nakhom Ratchasima	2.50	2.54	0.49
	Burirum	12.62	12.52	2.45
	Surin	11.20	11.23	2.17
	Sisaket	33.11	32.98	6.42
	Ubon Ratchathani	5.10	5.15	0.99
N	Yasothon	3.88	4.00	0.75
O	Chaiyaphum	2.06	2.12	0.40
R	Amnat Charoen	4.34	4.95	0.84
T	Nong Bua Lam Phu	2.01	2.83	0.39
H	Khon Kaen	13.48	13.45	2.61
E	Udon Thani	6.61	6.65	1.28
A	Loei	9.78	9.63	1.90
S	Nong Khai	8.45	8.21	1.64
T	Maha Sarakhom	4.69	4.84	0.91
	Roi Et	4.73	4.82	0.92
	Kalasin	34.03	33.76	6.60
	Sakon Nakhon	2.25	2.32	0.44
	Nakhon Phanom	4.03	4.13	0.78
	Mukdahan	6.56	6.62	1.27
	Nakhon Sri Thammarat	5.56	5.48	1.08
	Krabi	1.49	1.84	0.29
	Phangnga	15.08	14.30	2.92
	Phuket	6.65	7.95	1.29
S	Surat Thani	1.67	1.76	0.32
O	Ranong	3.34	3.36	0.65
U	Chumphon	1.46	1.49	0.28
T	Songkhla	4.40	4.64	0.85
H	Satun	4.62	5.01	0.90
	Trang	8.40	7.68	1.63
	Phatthalung	4.77	5.11	0.92
	Pattani	6.29	6.13	1.22
	Yala	2.56	3.30	0.50
	Narathiwat	8.63	8.25	1.67

Table A6 Raw and SEB smoothed incidence rates and excess risks by province, 2008.

Region	Province	Raw Incidence Rate (per 100,000)	SEB Smoothed Incidence Rate (per 100,000)	Excess Risk
	Bangkok	0.26	0.22	0.04
	Samut Prakarn	0.00	0.22	0.00
	Nonthaburi	0.10	0.12	0.01
	Pathum Thani	0.33	0.35	0.05
	Phra Nakhon Sri Ayuthay	3.01	2.81	0.45
	Ang Thong	0.70	0.94	0.11
	Lop Buri	1.06	1.65	0.16
	Sing Buri	1.39	1.44	0.21
	Chai Nat	8.32	7.74	1.25
	Saraburi	2.91	2.82	0.44
C	Chon Buri	0.56	0.58	0.08
E	Rayong	1.02	1.07	0.15
N	Chanthaburi	11.07	10.76	1.66
T	Trat	1.81	3.03	0.27
R	Chachoengsao	0.30	0.32	0.05
A	Prachin Buri	1.09	1.45	0.16
L	Nakhom Nayok	1.20	1.54	0.18
	Sa Kaeo	1.48	1.57	0.22
	Ratchaburi	0.12	0.16	0.02
	Kanchanaburi	1.79	1.75	0.27
	Suphanburi	0.36	0.43	0.05
	Nakhon Pathom	0.00	0.05	0.00
	Samut Sakhon	0.00	0.20	0.00
	Samut Songkhram	0.00	0.10	0.00
	Phetchaburi	0.22	0.15	0.03
	Prachuap Khiri Khan	0.20	0.32	0.03
	Chiang Mai	1.56	1.62	0.23
	Lamphun	0.00	0.41	0.00
	Lamphang	5.20	5.18	0.78
	Uttaradit	4.52	4.54	0.68
	Phrae	2.80	2.99	0.42
	Nan	16.57	16.25	2.49
N	Phayao	16.63	16.09	2.50
O	Chiang Rai	7.75	7.71	1.16
R	Mae Hong Son	2.76	1.79	0.41
T	Nakhon Sawan	1.58	1.64	0.24
H	Uthai Thani	5.81	5.35	0.87
	Kamphaeng Phet	0.69	1.31	0.10
	Tak	2.06	2.06	0.31
	Sukhothai	1.32	1.58	0.20
	Phitsanulok	2.61	2.64	0.39
	Phichit	1.80	1.92	0.27
	Phetchabun	3.71	3.76	0.56

Table A6 (Continued).

Region	Province	Raw Incidence Rate (per 100,000)	SEB Smoothed Incidence Rate (per 100,000)	Excess Risk
	Nakhom Ratchasima	3.60	3.61	0.54
	Burirum	46.98	46.85	7.06
	Surin	17.25	17.28	2.59
	Sisaket	22.47	22.29	3.37
	Ubon Ratchathani	7.20	7.25	1.08
N	Yasothon	3.15	3.38	0.47
O	Chaiyaphum	4.10	4.15	0.62
R	Amnat Charoen	4.88	5.12	0.73
T	Nong Bua Lam Phu	0.60	1.37	0.09
H	Khon Kaen	19.50	19.48	2.93
E	Udon Thani	10.96	11.00	1.65
A	Loei	27.55	27.09	4.14
S	Nong Khai	9.51	9.51	1.43
T	Maha Sarakhom	6.30	6.48	0.95
	Roi Et	6.27	6.36	0.94
	Kalasin	38.96	38.68	5.85
	Sakon Nakhon	2.87	2.93	0.43
	Nakhon Phanom	1.43	1.60	0.22
	Mukdahan	2.08	2.21	0.31
	Nakhon Sri Thammarat	15.76	15.63	2.37
	Krabi	1.45	1.77	0.22
	Phangnga	24.96	24.26	3.75
	Phuket	4.98	7.95	0.75
S	Surat Thani	2.56	2.70	0.38
O	Ranong	15.41	14.89	2.31
U	Chumphon	4.97	4.90	0.75
T	Songkhla	4.36	4.42	0.66
H	Satun	2.79	4.24	0.42
	Trang	4.08	4.28	0.61
	Phatthalung	4.96	5.14	0.75
	Pattani	2.81	3.89	0.42
	Yala	3.17	3.89	0.48
	Narathiwat	4.47	3.55	0.67

Table A7 Raw and SEB smoothed incidence rates and excess risks by province, 2009.

Region	Province	Raw Incidence Rate (per 100,000)	SEB Smoothed Incidence Rate (per 100,000)	Excess Risk
CENTRAL	Bangkok	0.16	0.16	0.02
	Samut Prakarn	0.52	0.34	0.06
	Nonthaburi	0.00	0.02	0.00
	Pathum Thani	0.00	0.03	0.00
	Phra Nakhon Sri Ayuthay	3.12	2.92	0.37
	Ang Thong	1.05	1.07	0.12
	Lop Buri	0.27	0.70	0.03
	Sing Buri	0.00	0.28	0.00
	Chai Nat	7.74	7.04	0.91
	Saraburi	0.80	0.98	0.10
	Chon Buri	0.47	0.49	0.06
	Rayong	0.67	0.72	0.08
	Chanthaburi	9.65	9.33	1.14
	Trat	1.80	3.05	0.21
	Chachoengsao	0.00	0.02	0.00
	Prachin Buri	0.00	0.45	0.00
	Nakhom Nayok	0.80	1.06	0.09
	Sa Kaeo	2.96	3.05	0.35
	Ratchaburi	0.12	0.17	0.01
	Kanchanaburi	2.62	2.47	0.31
	Suphanburi	0.36	0.44	0.04
	Nakhon Pathom	0.00	0.04	0.00
	Samut Sakhon	0.21	0.17	0.03
	Samut Songkhram	1.03	0.43	0.12
	Phetchaburi	0.00	0.17	0.00
	Prachuap Khiri Khan	0.60	0.65	0.07
NORTH	Chiang Mai	3.11	3.12	0.37
	Lamphun	0.00	0.76	0.00
	Lamphang	3.26	3.29	0.39
	Uttaradit	3.66	3.77	0.43
	Phrae	3.88	4.01	0.46
	Nan	18.49	18.08	2.18
	Phayao	14.98	14.63	1.77
	Chiang Rai	5.30	5.29	0.63
	Mae Hong Son	4.75	3.73	0.56
	Nakhon Sawan	2.70	2.70	0.32
	Uthai Thani	3.05	2.93	0.36
	Kamphaeng Phet	2.07	2.23	0.24
	Tak	0.74	1.48	0.09
	Sukhothai	1.82	2.13	0.22
	Phitsanulok	4.98	5.00	0.59
	Phichit	3.79	3.66	0.45
	Phetchabun	4.12	4.17	0.49

Table A7 (Continued).

Region	Province	Raw Incidence Rate (per 100,000)	SEB Smoothed Incidence Rate (per 100,000)	Excess Risk
	Nakhom Ratchasima	5.22	5.24	0.62
	Burirum	41.64	41.54	4.92
	Surin	44.85	44.73	5.30
	Sisaket	42.67	42.56	5.04
	Ubon Ratchathani	12.03	12.07	1.42
N	Yasothon	2.60	2.85	0.31
O	Chaiyaphum	5.17	5.21	0.61
R	Amnat Charoen	8.39	8.65	0.99
T	Nong Bua Lam Phu	3.60	4.31	0.43
H	Khon Kaen	19.36	19.34	2.29
E	Udon Thani	13.28	13.32	1.57
A	Loei	33.80	33.23	3.99
S	Nong Khai	7.39	7.45	0.87
T	Maha Sarakhom	9.82	10.06	1.16
	Roi Et	10.63	10.74	1.26
	Kalasin	24.32	23.86	2.87
	Sakon Nakhon	6.63	6.72	0.78
	Nakhon Phanom	1.14	1.64	0.14
	Mukdahan	10.67	10.64	1.26
	Nakhon Sri Thammarat	8.33	8.32	0.98
	Krabi	1.91	2.11	0.23
	Phangnga	36.81	36.71	4.35
	Phuket	7.95	7.95	0.94
S	Surat Thani	4.07	4.09	0.48
O	Ranong	123.68	122.83	14.61
U	Chumphon	1.65	1.68	0.20
T	Songkhla	6.51	6.55	0.77
H	Satun	9.71	9.74	1.15
	Trang	7.64	7.74	0.90
	Phatthalung	22.77	21.79	2.69
	Pattani	3.11	3.82	0.37
	Yala	4.42	4.89	0.52
	Narathiwat	8.47	8.07	1.00

APPENDIX B

ACCURACY ASSESSMENT OF MODIS IMAGE CLASSIFICATION

An important step in image classification process is the accuracy assessment. This step was done in order to determine how effectively pixels were grouped into the correct feature classes. The feature of interest of this study is the inundated areas which could be the source of leptospirosis infective agents. The extracted images were therefore classified into 2 classes, i.e., inundated area, and the others. In the extracted imaged the pixels classified as ‘inundated area’ were valued as ‘1’ and the pixels classified as ‘others’ were valued as ‘0’. These images require validation with the standard data.

The standard data used as the reference for accuracy was derived from a map of water body of L7018 series, scale 1:50,000. This map was rasterized using the cell size of the same as pixel size of MODIS extracted images, i.e., 458 meters The computer software, ERDAS Imagine 9.0 was used to assess the classification accuracy. Figure B1 illustrates the classified image and reference image

A stratified random sampling was used as method for the selection of testing points. Ninety points of inundated areas and ninety points of other area were randomly selected by the utility of software. This utility generated the reports of error matrix, accuracy and kappa statistics which were illustrated in Table B1 and Table B2.

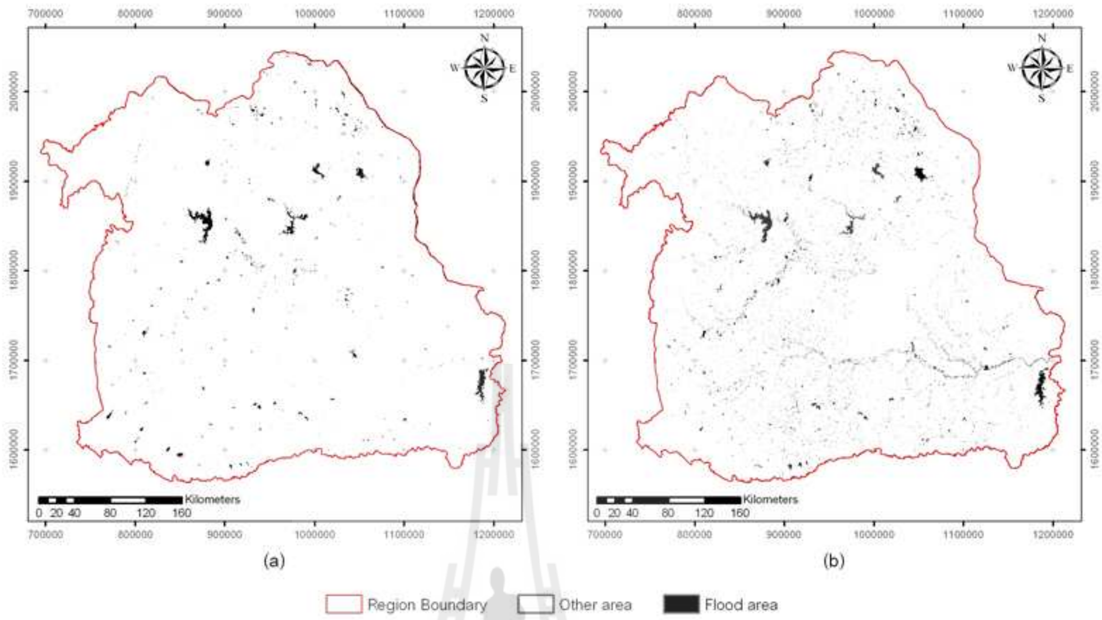


Figure B1 Image of water bodies and inundated area extracted from MODIS (a), and a raster map of water body from L7018 map series. (b).

Table B1 Error Matrix of classified data and reference data.

	Reference Data		
Classified Data	**Inundated area**	**Others**	**Total**
Inundated areas	77	13	90
Others	1	89	90
Total	78	102	180

Table B2 Accuracy and kappa statistics.

Class Name	Reference Totals	Classified Totals	Number Correct	Producers Accuracy	Users Accuracy
Inundated areas	78	90	77	98.7%	85.5%
Others	102	90	89	---	---
Totals	180	180	166		

Overall Classification Accuracy = 92.22%

Kappa Statistics

Overall Kappa Statistics = 0.844

Conditional Kappa for each Category

Class Name	**Kappa**
Inundated areas	0.745
Others	0.974

Overall accuracy of 92.2 percent was achieved, where the producer and user accuracy were 98.7 and 85.5 percent, respectively. The overall kappa value was 0.84. Kappa value of inundated areas was 0.74. According to the agreement criteria for Kappa statistic defined by Landis and Koch (1987), the agreement is poor when Kappa<0.4, good when 0.4<Kappa<0.7 and excellent when Kappa>0.75. This indicates that the agreement in the classification of inundated area is good.

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